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 CLAIMS

[Claim(s)]

[Claim 1] The constituent as the medical application which has the viscosity of 5,000cP(s) at least at 37 degrees C, and does not crystalize tidily under a perimeter or physiological conditions, but contains the high viscosity liquefied carrier material of nonaqueous solubility with a non-polymer, or a device for surgery.

[Claim 2] The constituent according to claim 1 whose high viscosity liquefied carrier material of nonaqueous solubility is cane-sugar acetic-acid isobutyric-acid ester in a non-polymer.

[Claim 3] The constituent according to claim 2 in which the liquefied carrier material of nonaqueous solubility exists to the AUW of a constituent in about 99.5 % of the weight - about 10% of the weight of an amount with a non-polymer.

[Claim 4] The constituent according to claim 2 in which the liquefied carrier material of nonaqueous solubility exists to the AUW of a constituent in about 95 % of the weight - about 25% of the weight of an amount with a non-polymer.

[Claim 5] The constituent according to claim 2 in which the liquefied carrier material of nonaqueous solubility contains a meltable solvent further with a non-polymer.

[Claim 6] The constituent according to claim 5 chosen from the group which the solvent which contains the liquefied carrier material of nonaqueous solubility with a non-polymer becomes from ethanol, dimethyl sulfoxide, ethyl lactate, ethyl acetate, benzyl alcohol, a triacetin, 2-pyrrolidone, N-methyl pyrrolidone, propylene carbonate, the Glico furol, and the aerosol propellants of arbitration.

[Claim 7] The constituent according to claim 5 with which the solvent which contains the liquefied carrier material of nonaqueous solubility with a non-polymer exists to the weight of a constituent in about 10 % of the weight - about 50% of the weight of an amount.

[Claim 8] The constituent according to claim 2 with which the constituent which contains the liquefied carrier material of nonaqueous solubility with a non-polymer contains an additive further.

[Claim 9] The constituent according to claim 8 with which the additive which contains the liquefied carrier material of nonaqueous solubility with a non-polymer is chosen from a biodegradability polymer, a non-biodegradability polymer, natural oil, synthetic oil, a carbohydrate, a carbohydrate derivative, mineral, and an inactive organic compound.

[Claim 10] The constituent according to claim 8 with which the additive which contains the liquefied carrier material of nonaqueous solubility with a non-polymer exists to the AUW of a constituent in the amount of about 1 % of the weight - about 20% of the weight of the range.

[Claim 11] The constituent according to claim 1 with which a constituent also contains the biological active substance for the controlled emission.

[Claim 12] A constituent [useful / as a conglutination agent of an organization / as allowance material of a wound as SUKAHORUDEINGU / in / for hemostasis / for restoration of the opening of a body tissue for the block of a device of surgical adhesion, and / a body tissue] according to claim 1 to 11. [a rebirth of an induction organization]

[Translation done.]

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DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

This invention relates to a high viscous liquid constituent useful for sending out of the matter, and other applications including covering of an organization, and prevention of adhesion.

[0002]

Background of invention Extensive research has been made in the field of the biodegradability sustained-release (control DORERIZU) system for a biological activity compound. The biodegradability matrix for sending out of drugs is useful in order that they may remove the need of removing the device with which drugs were drained.

[0003]

The most ordinary matrix material for sending out of drugs is a polymer. Since composition and biodegradability of polylactic acid were reported by KURUKARUMI etc. in 1966 ("the polylactic acid for the implant for surgery", Arch.Surg.93:839), the field of a biodegradability polymer has developed quickly. The example of other polymers reported to be useful as a matrix material for a sending-out device includes polyester like the Pori anhydride, poly glycolide, and a poly lactide-KOGURI corridor, polyamino acid like the poly lysine, the polymer of polyethylene oxide and a copolymer, acrylic end polyethylene oxide, a polyamide, polyurethane, poly ortho ester, a polyacrylonitrile, and polyphosphazene. For example, please refer to Langer's U.S. Pat. No. 4,891,225 and said 4,906,474 numbers (Pori anhydride), U.S. Pat. No. 4,767,628 (poly lactide and poly lactide-KOGURI corridor acid) of HATCHINSON, and U.S. Pat. No. 4,530,840 (the poly lactide, poly glycolide, and copolymer) besides Tais.

[0004]

It is common knowledge, the resolvability ingredient, for example, the bridge formation gelatin, of the biological origin. The bridge was constructed over hyaluronic acid and it was used as a resolvability bloating tendency polymer for a biomedical application (U.S. Pat. No. 4,957,744; (1991) "the surface denaturation of the polymer biomaterial for the thrombogen plasticity which decreased" besides DERRA BARRE, Polym.Mater.Sci.Eng.62:731-735).

[0005]

Moreover, it was developed in order that a biodegradability hydrogel might use it for sending out of the drugs adjusted as a carrier of hormone, an enzyme, an antibiotic, anticancer drugs, and a biological active substance like cell suspension. The deer was carried out and the local organization of temporary preservation of the functional property of the supported chemical species and these chemical species or the adjusted emission to systemic circulation was attained. For example, please refer to Cohen's U.S. Pat. No. 5,149,543. The film which has the permeability, the pore dimension, and catabolic rate of a certain suitable range for various kinds of applications in surgery, medical diagnosis, and a therapy by suitable selection of hydrogel 15 macromere can be made to generate.

[0006]

Current use is carried out as a carrier of the matter, especially a biological activity compound, or it

searches for many dispersing element systems for use. the dispersing element system used for medicine manufacture and a cosmetics formula object -- suspension -- or it can classify into either of the emulsions. The magnitude by which suspension was distributed in the liquefied medium using suspension is defined as being the solid particulate of the range from several nm to hundreds of micro. a solid particulate -- a microsphere and a microcapsule -- and NANOSU fair ***** is carried out. While was stabilized with the surface film of a surfactant or an emulsifier like a lipid, and an emulsion is defined as that by which the liquid is distributed in the liquid of another side. A water-in-oil type and oil-in-water type emulsion, a multiple emulsion, microemulsion, a micro drop, and liposome are included by the emulsion formula object. A micro drop is the phospholipid vesicle of the shape of a homogeneity layer which consists of a globular form-like lipid layer and an internal oil reservoir as defined as Hines's U.S. Pat. No. 4,622,219 and said 4,725,442 numbers. Liposome is a phospholipid vesicle prepared by mixing water-insoluble nature polar lipid with a water solution. The reverse entropy produced by mixing an insoluble lipid in water makes the advanced assembly of this cardiac sealing film of phospholipid, and the caught water solution generate.

[0007]

U.S. Pat. No. 4,938,763 besides Dan is indicating the approach of dissolving the water-insoluble nature thermoplasticity polymer of non-reactivity in the water-soluble solvent of biocompatibility, making a liquid forming, and making the implant forming on the spot by arranging this liquid inside of the body, carrying out stripping of the solvent, and making the solid-state implant generating. A polymer solution can be arranged inside of the body with a syringe. The implant can present the configuration of the cavity of the perimeter. By another example, the implant is formed from the reactant liquefied oligomer polymer which does not contain a solvent, and usually hardens by addition of a curing catalyst in a proper place, and forms a solid-state.

[0008]

Although it was evaluated in order that many ingredients might use it for the controlled delivery (adjusted sending out) of the matter, the need for providing that it is also at low toxicity about the easier system for the controlled delivery of the matter still exists. For example, the above-mentioned delivery system requires manufacture of the complicated constituent with weak ** of a polymer and the polymer matrix by which the load was carried out, a hydrogel, or others. A prescription is easily written with the matter which it is going to send out especially, and the need of offering the delivery system which used as the base the liquid easily prescribed for the patient exists.

[0009]

Therefore, the purpose of this invention is offering the simple system for sending out the matter. Other purposes of this invention are offering the delivery system which used as the base the liquid prescribed for the patient easily [a prescription is easily written with the matter which it is going to send out, and].

Other purposes of this invention are offering the approach for the controlled delivery of the matter in the system of the simple liquid base.

[0010]

Outline of invention According to this invention, it has the viscosity of 5,000cP(s) at least at (i)37 degree C, and the constituent as the medical application containing the matter which it is going to (ii) ii [the high viscosity liquefied carrier material (HVLCM) of nonaqueous solubility and / optional] Send out with the non-polymer which is not tidily crystallized under a perimeter or physiological conditions, or a device for surgery is offered.

[0011]

In one example, HVLCM by viscosity-down nature The solvent of water solubility or a water miscibility, For example, ethanol, dimethyl sulfoxide, ethyl lactate, ethyl acetate, Benzyl alcohol, a triacetin, 2-pyrrolidone, N-methyl pyrrolidone, Propylene carbonate, the Glico furol, Freon (for example, Tori Krol Fluor methane and dichloro Fluor methane), Wood ether, a propane, butane, dimethylformamide, dimethylacetamide, A diethylene glycol, a butylene glycol, N-(beta-hydronalium methyl) RAKUTO amide, It is mixed with dioxolane, other amides, ester, the ether, and alcohol, low

viscosity liquefied carrier material (LVLCM) is formed, and before this prescribes a medicine for the patient with the matter which it is going to send out, it is mixed. By the desirable example, LVLCM has the viscosity of 1000 or less cPs. if a medicine is prescribed for the patient -- a constituent -- the inside of the body -- or it is arranged on a front face, a solvent is emitted or spread from LVLCM, and the implant or constituent of high viscosity to which the matter is made to emit all the time in the location is made to form By selecting a solvent and HVLCM suitably, the viscosity of the constituent before various administration and after administration can be attained. By the desirable example, HVLCM is biodegradability.

[0012]

By one example, the matter mixed with HVLCM is a biological active substance useful for people's therapy, a veterinary medicine-therapy, or the agricultural purpose. In an agricultural field, a constituent is applicable to an appropriate location with a suitable activator for extermination (for example, DAIKUATO) of weeds, extermination (for example, methyl parathion) of an insect, or extermination of a noxious insect. In the field of veterinary medicine, since the mixed steroid as a growth promotor of a cow is sent out, a constituent can be used in order to send out a vaccine (for example, parvovirus vaccine of the sake after parent protection of a pig). a SUKAHORUDEINGU (making a scaffold) since in the case of people it can use it since a constituent sends out various biological active substances explained to a detail to below, or surgical adhesion is blocked apart from this sake -- the matter for playback of an induction organization for restoration of an opening, for example, *****, sake -- an activator -- or it was able to be used without the activator. In another example, a constituent can be poured into the artery supply route of a neoplasm, and it will form the high viscosity implant which bars the blood supply of a neoplasm there. another example -- a constituent -- a suture -- or it can be used without it as an organization conglutination agent. In still more nearly another example, a constituent can be used as partial covering for electric shielding for a wound.

[0013]

The implant for in vivo one of a constituent can be arranged to in the living body [somewhere in] including a coelome, the parodontal pocket, or a pocket like the coecum of an eye including muscles or an elasticity organization like a fat, a hard organization like a bone, *****, the oral cavity, a vaginal cavity, a rectum cavity, or a nasal cavity (not limited to these).

[0014]

A constituent contains optionally the additive which denatures the property of a constituent as a request. The organic salt like a biodegradability polymer, a non-biodegradability polymer, natural oil or synthetic oil, a carbohydrate or a carbohydrate derivative, mineral, BSA (bovine serum albumin), a surfactant, an organic compound like a saccharide, and citric acid sodium as an example which is not restrictive as for a suitable additive is included. Generally, it reduces the emission rate of the matter greatly compared with the same constituent without an additive, so that an additive is not water solubility (i.e., so that it is oleophilic). It is desirable to use the additive which increases the reinforcement of a constituent or a property like porosity by one example. Furthermore, by a certain example, it is used combining an additive, without using the matter which HVLCM or LVLCM tends to send out.

[0015]

By another example, it is contained in the second carrier material since HVLCM / substrate constituent makes storage, handling, and sending out easy, or in order to denature one or more of the properties of a constituent again. The examples which are not restrictive as for the second carrier material are the liquid whose HVLCM is not fusibility (an emulsion is formed), a solid-state, a gel formula object, and an endermic sending-out system. This substrate should have low solubility for high solubility in HVLCM at the second carrier material.

For example, the underwater emulsion of HVLCM/substrate can be offered. The useful emulsion included in the range of this invention is a gargle which is an activator for a substrate to treat ozostomia, the infectious disease in opening, or other opening internal derangement damage. By another example, HVLCM is used as a carrier for partial administration of the matter.

For example, HVLCM can make the solubility of a biological activator, and endermic transportation

support. In another example, HVLCM was able to be used as a carrier for the insectifuga containing DEET. In still more nearly another example, HVLCM is used for chemicals, for example, a louse eliminator, or advancing and sending out an inhibitor compound or the compound for a therapy to hair or the scalp.

[0016]

Selection of the concrete explanation I. high viscosity liquefied carrier material of invention It is nonaqueous solubility in a non-polymer, and it has the viscosity of 5,000cP(s) (by the case, it is 10,000, 15,000, 20,000, 25,000, or 50,000cP(s) at least, and skill is good) at least at 37 degrees C, and the high viscosity liquefied carrier material which is not tidily crystallized under a perimeter or biological conditions should be selected. The vocabulary "nonaqueous solubility" means the ingredient which is water solubility to 1 or less % of the weight of extent under ambient conditions.

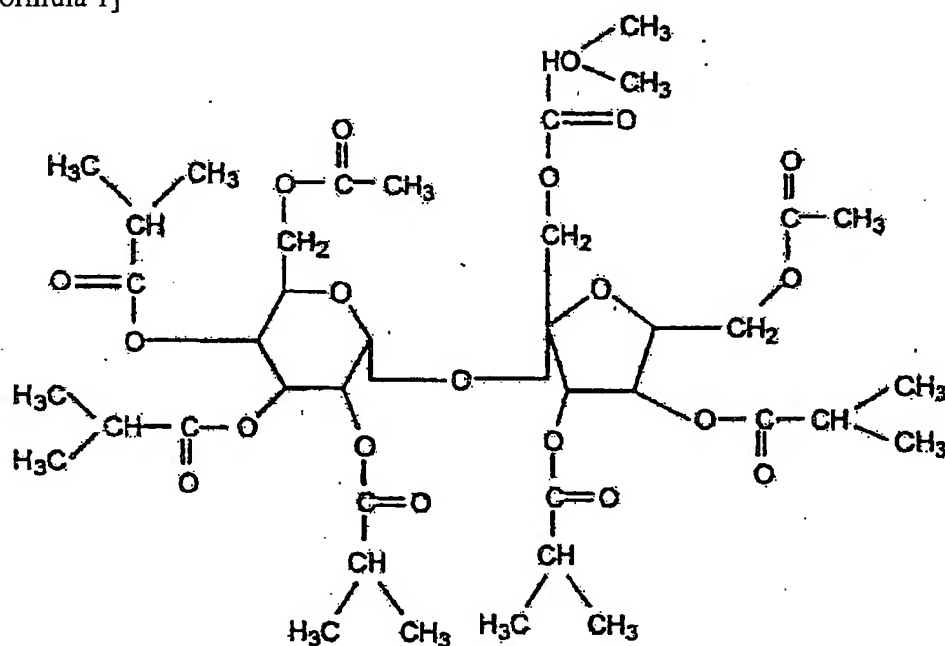
[0017]

Viscosity falls to dominance and HVLCM makes LVLCM mixable with a substrate for a controlled delivery form by the desirable example, when it mixes with a solvent. LVLCM / substrate constituent is easier to arrange inside of the body than HVLCM / substrate constituent typically. That is because it can flow easily for a syringe or other transplantation means, it can flow out of it easily and a prescription can be easily written as an emulsion. LVLCM can have the viscosity of a request of arbitration. About 1000 or less cPs were understood that the viscosity range of LVLCM of 200 or less cPs is typically useful in more detail for application by in vivo one.

[0018]

By the desirable example, the cane-sugar acetic-acid isobutyric-acid ester ("SAIB") which is the cane-sugar molecule esterified by two acetic-acid parts and six isobutyric-acid parts is used as HVLCM. The structure of SAIB is shown below.

[Formula 1]



[0019]

SAIB is nontoxic in taking orally, and current is used in order to stabilize an emulsion in food stuff industry. It is a very viscous liquid and has the unusual property in which there is a dramatic change of viscosity by grant of little heat, or addition of a solvent. It is fusibility at the solvent of much biocompatibility. When it has the shape of a solution or an emulsion, SAIB can be applied with injection or an aerosol spray. SAIB(s) are the cellulose ester which may influence the sending-out rate of the matter, and other polymers and compatibility.

other examples -- HVLCM -- the stearic-acid-ester; octadecanamide of stearic acid ester, for example, propylene glycol, glyceryl, a diethylaminoethyl, and a glycol and other long-chain-fatty-acid amides, for example, N, and N' -- they can be - ECHIRENJI stearamide, Stearamide MEA and DEA, ethylene-bis-stearamide, cocoa MINOKISHIDO; long-chain fatty alcohol, for example, cetyl alcohol, and stearyl alcohol; long-chain ester, for example, myristic-acid Millis Chill, erucic-acid behenyl, and glyceryl phosphate. By the specific example, HVLCM is acetylation cane-sugar distearate (clo DESUTA A-10).

[0020]

HVLCM exists in a constituent in the amount of the arbitration which makes the effect of desired attain. For example, for prevention of adhesion, HVLCM can be independently used as a protection film or bolus as covering of an organization with the substrate which heightens the property or effectiveness of the matter. About 95% - 25% of HVLCM(s) exists in about 85% - 45% of amount most typically still more preferably to the AUW of a constituent in a controlled delivery constituent from about 99.5% to about 10 % of the weight.

[0021]

Matter which it is going to II. Send out Any matter in which a desired property is shown can be sent out using this approach. Preferably, this matter is a biological active substance.

With the vocabulary "a biological active substance", when using it here The drugs which produce biological effectiveness when birds and the animal (not limited to these) containing mammals including people are medicated by in vivo ones, A peptide, protein, a carbohydrate (monosaccharide, oligosaccharide, and polysaccharide are included), Nucleoprotein, mucoprotein, lipoprotein, synthetic polypeptide, or protein, Or the small molecule combined with protein, glycoprotein, a steroid, a nucleic acid (cDNA, RNA, or those fragments are included, and it is the form of the arbitration of DNA), A nucleotide, an oligonucleotide (antisense oligonucleotide), a gene, a lipid, hormone, a vitamin (IG vitamin C and vitamin E are included), or an organic molecule including these combination is said.

[0022]

The vocabulary "drugs" means the interior or the matter of arbitration used externally as drugs for the therapy of the illness or a failure, treatment, or prevention, when using it here. An immunosuppressant, an anti-oxidant, a narcotic, a chemotherapeutic drug, a steroid (a retinoid is included), Although radiation absorbents including hormone, an antibiotic, an antiviral, an antimicrobial agent, a growth inhibitor, an antihistamine, an anticoagulant, an optical antioxidant, a MERANOTORO pick peptide, a non-steroid system and a steroid system anti-inflammatory compound, an antipsychotic drug, and UV absorbent are contained It is not limited to these.

[0023]

Moreover, an insecticide, agricultural chemicals, a germicide, a rodenticide, a vegetable nutrient, and a growth promotor are also included with the vocabulary "a biological active substance."

[0024]

In one example, a constituent is a vaccine and the matter which it is going to send out is an antigen. An antigen can be guided from a cell, bacteria, virions, or those parts. Antigens may be protein, a peptide, polysaccharide, glycoprotein, a glycolipid, nucleic acids, or such combination, when using it here, and these lengthen an immunogenicity response to an animal, for example, mammalian, birds, or fishes, and make them come out. When giving a definition here, an immunogenicity response is humoral or a cell may mediate it. the reagent kit which it uses a standard covalent-bond technique, for example, can come to hand commercially [some] when the matter to which it is going to lead an immunogenicity response is lacking in antigenic -- a carrier like albumin -- or conjugation can be carried out to hapten.

The example of a desirable antigen is influenza protein, human immunodeficiency virus (HIV) protein and A and B or viral protein like hepatitis C protein, a gram-negative bacterial cell wall, and Neisseria. A lipopolysaccharide like gonorrhea protein and a parvovirus are included.

[0025]

An antiinfective drug [like nitrofurazone and sodium propionate] whose example which is not restrictive as for the pharmacology-matter is; Penicillin, A tetracycline, oxytetracycline, chlorotetracycline, Bacitracin, a nystatin, streptomycin, a neomycin, a polymyxin, Gramicidin, a

chloramphenicol, an erythromycin, and azithromycin are included. An antibiotic; sulfo acetamide, sulfamethizole, the sulfamethazine, sulfadiazine, a sulfamerazine, and a SURUFU isoxazole -- including -- sulfonamide; -- the id -- chestnut gin -- including -- an antiviral; antiallergic agent -- For example, antazoline, a meta-pilus ten, chlorpheniramine, mepyramine, Pro FEMPIRIDAMIN, hydrocortisone, cortisone, hydrocortisone acetate, Dexamethasone and dexamethasone 21-phosphate, fluocinolone, triamcinolone and a prospect -- RISON, prednisolone, and prednisolone 21-sodium succinate and prednisolone acetate; hyposensitization medicine -- For example, a ragweed pollen antigen, a hay fever antigen, a dust antigen, and a milk antigen; A vaccine, For example, the smallpox, yellow fever, distemper, a swine fever, varicella, an antitoxin, Scarlet fever, diphtheria toxoid, tetanus toxoid, ****, pertussis, Influenza rabies, mumps, measles, polio, and Newcastle disease; Congestion removal medicine, For example, phenylephrine, naphazoline, and tetra-hydrazo phosphorus; A miotic and anticholinesterase, For example, pilocarpine, ESUPE phosphorus salicylate, carbachol, fluorophosphoric acid diisopropyl, Phospholine iodide and a demecarium bromide; A parasympatholytic drug, for example, atropine sulfate, Cyclopentolate, homatropine, scopolamine, tropicamide, Eucatropine and hydroxyamphetamine; The sympathetic agent, for example, an epinephrine; sedative, and a hypnotic, For example, pentobarbital sodium, FENO eve ruby tar, secobarbital sodium, Codeine, a urea (alpha-bromine iso valeryl), carbromal; A psychic energizer, For example, 3-(2-aminopropyl) Indore acetate and 3-(2-amino butyl) Indore acetate; Tranquilizer, For example, reserpine, chlorpromazine, and thiopropazate; An androgen nature steroid, For example, methyltestosterone and a full ORIME sterone; Estrogen, For example, estrone, 17beta-estradiol, ethinylestradiol, and a diethyl SUCHIBE sterol; Progesterone Mr. drugs, Non [for example, / progesterone, megestrol, meringue SUTORORU and KURORU serious] The ethisterone, the norethynodrel, 19-norprogesterone, the norethindrone, Medroxyprogesterone and 17beta-hydroxyprogesterone; Humoral drugs, For example, a prostaglandin, for example, PGE1, PGE2, and PGF2;; An antipyretic, For example, aspirin, sodium salicylate, and salicylamide; Antispasmodic, Atropine, meta-anserine, papaverine, and methscopolamine bromide; Antimalarial, For example, 4-amino quinoline, 8-amino quinoline, a KURORU kinin, and pyrimethamine; An antihistaminic agent, For example, diphenhydramine, the dimenthhydrinate, a TORIPEREN amine, Perphenazine and KURORU phenazine; A cardioactive agent, for example, JIBENZU hydroflumethiazide, Flumethiazide, chlorothiazide, and amino TORETO; a nutrient, for example, a vitamin, nature, synthetic biological biologically active peptide, and protein (including a growth factor, a cell fusion factor, cytokine, and a biological response modifier) are included.

[0026]

An activity compound is contained in sufficient amount to send out an amount effective in making a host animal or vegetation attain desired effectiveness in a constituent. It depends for the amount of the drugs included in a constituent, or a biological activator on the concentration of the drugs required of a desired emission profile and biological effectiveness, and the emission period of a request of drugs.

[0027]

Moreover, it depends for the concentration of the activity compound in a constituent on the factor of others which were known by this contractor at absorption of drugs, inactivation, and an elimination rate list. Please recognize changing with the severity in the condition that you make it also mitigate the value of a dose. Furthermore, please understand that it is not what does not pass over the above-mentioned density range to instantiation, but restricts the range of the constituent of this invention, or operation to what should be adjusted over a long period of time according to each need and special decision of the patient in whom the resume of a specific dose receives directions of a receptacle or administration for administration of a constituent, and a list about the special patient of arbitration. One medication is sufficient as a constituent, or it may change a time interval and may divide it into several times of little dosage.

[0028]

Typically, about 0.5 % of the weight - about 20 % of the weight of biological active substances exists still more typically to the AUW in about 1 % of the weight - about 10% of the weight or more of the range in a constituent. Another desirable range is about 2 % of the weight - 10 % of the weight. Range

desirable about very activity drugs like a growth factor is 1 or less % of the weight and 0.0001 more% or less.

The both sides of the fusibility matter and the insoluble matter can be distributed in HVLCM or LVLCM for a controlled delivery.

[0029]

III. additive In order to denaturalize as a request of the property of the matter, HVLCM can add various kinds of additives optionally to LVLCM. An additive can exist in any sufficient amount to give a desired property to a constituent. Generally, the amount of the additive used is the class of additive, and the function of effectiveness which it is going to obtain, and a routine test can determine it easily. When it exists, an additive exists in a constituent to the AUW of a constituent in the amount of about 0.1 % of the weight - about 20% of the weight of the range typically, and exists still more typically in the amount of about 1, 2, or 5 % of the weight - about 10% of the weight of the range. Into a constituent, an additive of a certain kind like a buffer is little, and recognizes chisel existence.

Although the following category is the example of the class of additive which can be used for a constituent, it is not limited to these. If the purpose which is going to indicate and attain this invention is shown, if it is this contractor, in order to attain the desired purpose, it will know easily how other additives will be selected. It is thought that all these examples go into the range of this invention.

[0030]

A. Biodegradability polymer One of the categories of an additive is the polymer and oligomer of biodegradability. A polymer can be used for changing the emission profile of the matter which it is going to send out, and adding integrity to a constituent, or denaturing the property of a constituent. As an example which is not restrictive as for the polymer of suitable biodegradability, and oligomer Pori (lactide), Pori (lactide-KOGURI corridor), Pori (glycolide), Pori (caprolactone), a polyamide, the Pori anhydride, polyamino acid, Poly ortho ester, poly cyanoacrylate, Pori (phospho gin), Pori (phospho ester), polyester amide, the poly dioxane, polyacetal, The poly ketal, a polycarbonate, poly alt.carbonate, resolvability polyurethane, Polyhydroxy butyrate, polyhydroxyvalerate, a polyalkylene OKISA rate, polyalkylene succinate, Pori (apple acid), a chitin, chitosan, the copolymer of these matter, a ternary polymerization object, an oxycellulose, combination, or mixture is included.

As for the example of Pori (alpha-hydroxy acid), Pori (glycolic acid), Pori (DL-lactic acid), Pori (L-lactic acid), and these copolymers are contained. The example of poly lactone includes Pori (epsilon-caprolactone), Pori (delta-valerolactone), and Pori (gamma-butyrolactone).

[0031]

B. Non-biodegradability polymer Another additive for using it with the constituent of this invention is a non-biodegradability polymer. The example which is not restrictive as for the resolvability polymer which can be used as an additive includes polyacrylic ester, an ethylene-vinyl acetate polymer, a cellulose and a cellulosic, acylation cellulose acetate and its derivative, un-corroding nature polyurethane, polystyrene, a polyvinyl chloride, polyvinyl fluoride, Pori (vinyl imidazole), the Krol sulfonation polyolefine, and polyethylene oxide.

A desirable non-biodegradability polymer contains polyethylene, a polyvinyl pyrrolidone, an ethylene-vinyl acetate polymer, a polyethylene glycol, cellulose acetic-acid butylate ("CAP"), and cellulose acetic-acid propionic-acid ester ("CAP").

[0032]

C. An oil and fat The additive of another class which can be used for the constituent of this invention is the oil and fat of nature and composition. the oil guided from the nut and seed of an animal or vegetation -- typical -- a fatty acid -- the glyceride of oleic acid, a palmitic acid, stearin acid, and a linolenic acid is mainly contained. In principle, an oil becomes viscosity, so that a molecule contains much hydrogen. Suitable nature and the example which is not restrictive as for synthetic oil include vegetable oil, peanut oil, an inside chain triglyceride, soybean oil, an almond oil, olive oil, sesame oil, fennel oil, camellia oil, corn oil, castor oil, cotton seed oil, the soybean oil that is poor quality or was refined, and a medium-chain-fatty-acid triglyceride.

Typically, a fat is glyceryl ester of stearin acid and a higher fatty acid like a palmitic acid. Such ester and

those mixture are solid-states at a room temperature, and show crystalline structure. Lard and beef tallow are the example. Generally, an oil and a fat increase the hydrophobicity of SAIB and make decomposition and water absorption late.

[0033]

D. A carbohydrate and carbohydrate derivative The additives of another class which can be used for the constituent of this invention are a carbohydrate and a carbohydrate derivative. The example which is not restrictive as for these compounds contains polysaccharide in monosaccharide (simple sugar like a fructose and its isomer glucose (glucose)), disaccharide, for example, cane sugar, a maltose, a cellobiose and a lactose, and a list.

[0034]

IV. solvent When a constituent is used as LVLCM, it should contain the solvent whose HVLCM is fusibility. Preferably, the matter which it is going to send out is also fusibility at a solvent. A solvent should be not toxicity but water solubility, or a water miscibility, otherwise should be biocompatibility. The solvent which is toxicity should not be used for medicine manufacture or the agricultural purpose. The solvent used for pouring a constituent into an animal should not produce a stimulus or necrosis of a big organization by the part of transplantation (unless a stimulus or a necrosis is desired effectiveness). a solvent -- it -- body fluid -- or as it is quickly spread by other aquosity environments and they are made solidify a constituent or solidified, it should be water solubility at least. The example of a suitable solvent includes ethanol, ethyl lactate, propylene carbonate, the Glico furol, N-methyl pyrrolidone, 2-pyrrolidone, propylene glycol, an acetone, methyl acetate, ethyl acetate, a methyl ethyl ketone, benzyl alcohol, a triacetin, dimethylformamide, dimethyl sulfoxide, a tetrahydrofuran, a caprolactam, DESHIRU methyl sulfoxide, oleic acid, and 1-dodecylazacycloheptane-2-one.

When SAIB is used as HVLCM, desirable solvents are ethanol, dimethyl sulfoxide, ethyl lactate, ethyl acetate, benzyl alcohol, a triacetin, N-methyl pyrrolidone, propylene carbonate, and the Glico furol. SAIB(s) are not a glycerol, corn oil, peanut oil, 1, 2-propanediol, a polyethylene glycol (PEG200), super-purification sesame oil and super-purification peanut oil, and a miscibility. Therefore, the latter group's solvent is not desirable for using it with SAIB.

Typically, a solvent is added by the constituent to the AUW of a constituent in the amount of about 5 % of the weight - about 55% of the weight of the range. Preferably, a solvent exists in a constituent in the amount of about 10 % of the weight - about 50% of range. The desirable range is about 10 % of the weight - 30 % of the weight.

[0035]

V. Use of LVLCM and a HVLCM constituent A host can be medicated with the constituent indicated here by the various approaches of changing according to the result which it is going to attain. When a host is an animal like people, if a constituent is a request, a suitable carrier can be put in and medicated with it being locally, that it is systemic (in for example, membrane path (in taking orally, a rectum path, a vagina path, or nose path)), or parenterally (the inside of a vein, hypodermically, intramuscular, or intraperitoneal), for example. When a constituent is used for the agricultural purpose, it can be slushed and can be applied with spraying, immersion, aerosol, or a coater.

[0036]

desirable -- the purpose of medicine manufacture or veterinary medicine sake -- the constituent of this invention -- as a solution -- impregnation -- or a medicine is prescribed for the patient by aerosol, the paste, or the emulsion. When a medicine is prescribed for the patient by impregnation as LVLCM, covering for the organization which the small quantity of the solvent used for the constituent can exude [organization] in a host's aquosity fluid, and the storage area of high viscosity for the controlled delivery of the matter or adhesion can be blocked [organization], or can make it the minimum is made to form. It is aerosol, or when are used by the emulsion and the small quantity of the solvent in a solution is applied, it evaporates, and LVLCM is produced as HVLCM. Formation of aerosol and an emulsion can be attained using the technique known by this contractor. for example, "a medicine manufacture administration gestalt and the delivery system of drugs" besides ANSERUH.C. -- please refer to the 6th edition and 1995.

[0037]

A constituent can be used so that the protective covering of an organization may be formed, and it can be used for preventing especially formation of surgical adhesion. Since it ** by the ability adhering to a surrounding organization or a surrounding bone, and synthesis of the organization is carried out or it is filled up with a deficit, HVLCM can be injected into hypodermically like a collagen. Moreover, it can be poured in so that formation of a deep scar may be prevented to a wound including a burn. The resolving time of HVLCM can be adjusted as an additive to HVLCM using a polymer. Then, the implant formed of HVLCM is taken and replaced with this, when it biodegrades slowly in a body, and a natural organization is grown up and the implant disappears.

[0038]

Use as a device of VL.VLCM and HVLCM Various applications which are unrelated to the practicality of sending out of drugs are related with using it as a device in various medicine or surgical applications. One of the desirable examples of LVLCM and hHVLCM is SAIB. although that the practicality of the device for SAIB blocks surgical adhesion, being filled up with an opening, a rebirth (including hemostasis) of an induction organization, the conglutination agent of an organization, SUKAHORUDEINGU, and the allowance material of a wound are contained -- these -- it is not limited. Each of these applications can include emission of a biological active substance, or sending out of drugs by the case. For example, SAIB as allowance material of a wound holds various growth factors easily, and promotes recovery of a wound.

[0039]

In order to block surgical adhesion, the film with which it was sprayed or applied for blocking adhesion of resemblance or a different organ is suitable. the Freon of the aerosol propellants of ethanol, ethyl lactate, a N-methyl-2-pyrrolidone, or arbitration with ordinary SAIB, wood ether, or arbitration -- including -- either of the various solvents -- an additive -- or a prescription is written without an additive and it is applied as an aerosol spray. The obtained film can perform adhesion, condensation, decomposition, porosity, or those combination.

[0040]

For restoration of an opening, SAIB is typically suitable like the collagen for restoration on cosmetics. For the related application, SAIB can contain an anesthetic or an antibiotic, in order to carry out being [it / useful] and label-sending out to holding the bone chips in fracture collectively.

[0041]

Restoration of **** for blocking a rebirth of an induction organization, for example, the epithelial migration, is other application. Advantageously, the constituent of this invention is applied from a solution. Although various growth factors and cell reattachment factors are included by the typical drugs blended with these constituents for a rebirth of an induction organization, it is not limited to these.

[0042]

Typically, a halt of the hemostasis in a surgical setup or a blood flow is another practicality. The constituent of this invention is biodegradability. These are not limited although a suitable additive includes polyvinyl alcohol, a polyethylene glycol, or a carboxymethyl cellulose. A suitable solvent includes ethyl lactate and propylene glycol.

[0043]

The SAIB formula object sprayed or applied is suitable as an organization conglutination agent for closing of a wound as a main sealant at either of the combination with a suture or a staple. A suitable additive is a carboxymethyl cellulose or a polyvinyl pyrrolidone. Suitable solvents are propylene carbonate, ethyl lactate, the Glico furol, dimethyl sulfoxide, 2-pyrrolidone, a N-methyl-2-pyrrolidone, and ethanol. The biological active substance blended with these constituents for conglutination of an organization is not limited to these, although an antibiotic, an anti-inflammatory compound, a painkiller, an anesthetic, and a growth factor are contained.

[0044]

SUKAHORUDEINGU is another device practicality for the constituent of this invention, and can suit growth of a new organization especially. A typical formula object contains a polyvinyl pyrrolidone and

phosphoric acid TORINA thorium. SUKAHORUDEINGU offers the suitable matrix for adhesion and growth of a bone or a nerve cell. Although the biological active substance blended with these constituents for SUKAHORUDEINGU includes a growth factor, it is not limited to this.

[0045]

Other applications of the constituent of this invention are wound allowance material which does not blend or blend suitable drugs. Wound allowance material protects a wound and has the function to promote the process of recovery. In one of the typical applications, SAIB is applied as an aerosol spray. Although the biological active substance blended with these constituents in wound allowance material includes an antibiotic like amikacin, an anti-inflammatory compound, a painkiller, an anesthetic, or a growth factor like a fibroblast growth factor, it is not limited to these.

[0046]

Local oral delivery constituent If this invention is followed, the typical oral delivery system containing a surfactant, an oily component, HVLCM, for example, cane-sugar acetic-acid isobutyric-acid ester, and the water that can maintain sending out an activator to the oral cavity can be manufactured.

This invention can be used for prescribing the long-acting gargle which contains SAIB and an activator with an emulsion gestalt in the second carrier material which used water as the base. For example, if it is used as a practice before a gargle goes to bed, the next morning has reduction in ozostomia.

the component in a gargle formula object -- six group: antimicrobial activity agents, a surfactant, an auxiliary surfactant, an oily component, cane-sugar acetic-acid isobutyric-acid ester, and water -- and it can be alike and can divide into an additive. Each of these groups is explained below at a detail. If this indication is shown, this contractor can prepare the partial oral delivery systems of others for extensive application also including the therapy of oral infection and other oral cavity failures by selecting a suitable activator.

[0047]

Antimicrobial activity agent Although domiphen bromide, triclosan, chlorhexidine, essential oil, cetylpyridinium chloride, fluoride, alexidine, the salicylanilide, a zinc compound, and an antibiotic are included by the gargle formula object at the antimicrobial activity agent by which current use is carried out, it is not limited to these. These are independent, or can be combined and used. Cetylpyridinium chloride and a zinc compound, especially zinc gluconate are desirable.

[0048]

Surfactant Surfactant generally selected in order to use it for the constituent of this invention Although it is water solubility and nonionic and polyoxyethylene castor oil, polyoxyethylene hydrogenation castor oil, polyoxyethylene sorbitan fatty acid ester, polyoxyethylene alkyl ester, polyoxyethylene alkyl ether, polyoxyethylene glycerol ester, and a sorbitan fatty acid ester are included, it is not limited to these. these are independent -- or it is combined and used. A desirable nonionic surfactant is polyoxyethylene glyceryl ester which has the polyoxyethylene sorbitan fatty acid ester and the 5-20-mol ethylene oxide which have 5-40-mol ethylene oxide. Especially desirable things are polyoxyethylene (20EO) sorbitan monooleate, a polyoxyethylene (20EO) almond oil, polyoxyethylene (20EO) hydrogenation castor oil, etc.

The amount of the surfactant which should be blended with the constituent of this invention changes according to the class of surfactant to be used. Generally, although the desirable range is 60 % of the weight, especially the desirable range is 2 - 10 % of the weight.

[0049]

Auxiliary surfactant Generally the auxiliary surfactant used for the formula object of this invention is called the alcohol of a surfactant / auxiliary surfactant system, or the nonionic component of a low hydrophilic property / oleophilic balance (HLB). In the formula object of this invention, the auxiliary surfactant which has a function as a solubilizing agent or a cosolvent besides having a function as a surfactant is desirable. The alcohol or the nonionic surfactant of low HLB of univalent or many ** is independent as such an auxiliary surfactant, or can use it in two or more sorts of those combination. As an example of univalent alcohol, benzyl alcohol, ethyl alcohol, octyl alcohol, etc. are shown, and propylene glycol, glycerol, 1, and 3-butylene glycol etc. is shown as an example of the alcohol of many

** . As an example of the nonionic surfactant of low HLB, a distillation monoglyceride, polyglycerin poly oleate, and the polyethylene glycol of molecular weight 300-4,000 are shown. Polyglycerin poly oleate is shown as a still more desirable example of an auxiliary surfactant. Especially the thing contained in a desirable auxiliary surface active agent is decaglyceryl tetra-oleate.

The amount of these auxiliary surfactants that should be blended with the formula object of this invention changes according to the class of auxiliary surfactant to be used. Generally, the desirable range is 0.5 - 30 % of the weight, and especially the desirable range is 1 - 5 % of the weight.

[0050]

Oily component One or more sorts of oily components typically chosen from the group which consists of a glycerine fatty acid ester, fatty acid ester, fatty alcohol and those derivatives, a fatty alcohol benzoate, and a hydrocarbon can use it as an oily component in the formula object of this invention. Regardless of Monod who can approve, G, the Tori-glycerides, or those mixture, whether or not it will be natural, a composite compound, or the compound of a semisynthesis, it can be used for those sources of supply or origins as a glycerine fatty acid ester. A desirable glycerine fatty acid ester is a medium-chain-fatty-acid triglyceride, is independent in the almond oil which is either poor quality or purification, olive oil, sesame oil, peanut oil, fennel oil, camellia oil, corn oil, castor oil, cotton seed oil, soybean oil, and a list, or is combined and used for them. Especially a desirable thing is a medium-chain-fatty-acid triglyceride.

Desirable fatty acid ester is myristic-acid isopropyl, palmitic-acid octyl, ethyl oleate, and palmitic-acid ethyl. Especially desirable things are myristic-acid isopropyl and palmitic-acid octyl. Especially desirable fatty alcohol derivatives and fatty alcohol benzoates are 2-octyl dodecanol and a C25 alcoholic benzoate. ***** is shown as a hydrocarbon with desirable heavy liquefied paraffin.

An oily component is independent or can be used combining other oily components. These oily components can be preferably blended with the formula object of this invention in 1 - 10% of the weight of an amount 0.5 to 50% of the weight.

[0051]

Cane-sugar acetic-acid isobutyric-acid ester The cane-sugar acetic-acid isobutyric-acid ester explained to the detail in the top is used as HVLCM. SAIB is typically blended with a formula object in 0.1 - 2% of the weight of an amount preferably 0.01 to 10% of the weight.

[0052]

Water Other indispensable components of a gargle formula object are water. the formula object of this invention -- 3-10 -- desirable -- 5-9 -- it has pH of 6-8 still more preferably. A buffer can be used for maintaining pH of the above-mentioned range. an acetic acid, citric acid, phosphoric acid, benzoic acids, and (or) those salts are shown as an example of a desirable buffer. pH can be adjusted in the desirable range by adding a suitable acid or a suitable base, for example, a hydrochloric acid, or a sodium hydroxide during manufacture according to necessary accommodation. Moreover, deionization of the water used for the formula object of this invention is carried out, and being filtered is desirable.

[0053]

Additive Other component, for example, preservative, stabilizer, anti-oxidant, coloring agent, isotonicity agent, charge of flavor, wetting agents, sequestering agents, vitamins, vitamin precursors, etc. can be added if needed. As a desirable example of a preservative, a PARABAN derivative is shown and methyl PARABAN and propyl PARABAN are the most desirable preservatives. As a desirable example of an anti-oxidant, butylhydroxyanisole, butylhydroxytoluene, propyl gallate, vitamin A acetate, and a purification hydroquinone are shown, and vitamin A acetate and butylhydroxytoluene are shown as most desirable anti-oxidant. Sorbitol is shown as an example of a desirable wetting agent. Peppermint oil, spearmint oil, winter Green oil, menthol, and saccharin are shown as a desirable example of the charge of flavor. It is citric acid which is shown as a desirable example of a sequestering agent.

According to the approach of common use, a partial oral delivery system can blend an oil phase and the aqueous phase separately, and can manufacture them by making it coalesce at the temperature which had two phases subsequently raised. It is fully mixed, and the mixture of an oil phase and the aqueous phase is packed after being cooled by the room temperature.

[0054]

VII. example By the indication of this specification, if it is this contractor, an extensive HVLCM constituent can be manufactured and used. It is meant that these various examples go into the range of this invention. The following examples for making instantiation easy explain manufacture and use of a SAIB constituent to a detail. Other HVLCM(s), additives, substrates, and solvents can be used in the mode of resemblance of this appearance.

The constituent of the request in an example was manufactured using the following general procedures. a formula object is made from the scintillation bottle of 20mL(s), it shakes, and it stirred, and (or) it heated and the biological active substance was dissolved in SAIB / solvent system. In the example which a biological active substance does not dissolve, the formula object was refrigerated and stirred and it considered as the best distribution of a biological active substance by the drop.

[0055]

It opted for in vitro emission of a biological activity compound using the following general procedures. pH7.4 -- or the phosphate buffered saline ("PBS") (10mL) which is either of the pH6.8 was added in the 16x125mm test tube. pH of PBS which is 7.4 or 6.8 was selected based on the application and solubility of a biological active substance. PBS contained 0.2% of sodium azide, in order to prevent growth of a microorganism. SAIB / solvent / biological active substance formula object (0.03-0.09g) was emitted to disposable plastics pipet blank test tubing, and weight was recorded. It put into the shaking bath which makes a plug a test tube and carries out fixed shaking at 37 degrees C.

The test tube was periodically taken out from the shaking bath at the various times. At the time, PBS was taken out from the formula object containing a formula object, and it put into pure drying test tubing. These samples were analyzed and the amount of the biological active substance in an PBS solution was determined. New PBS was put into the test tube containing a formula object, and this was returned to the shaking bath. This operating procedure was repeated at the time of the versatility which obtains a sample.

The emission profile was plotted based on the original amount of the biological active substance in a formula object using the concentration of the biological active substance in an emission solution. This amount was determined using W visible spectrophotometry.

[0056]

Various solvents including ethanol (EtOH), dimethyl sulfoxide (DMSO), ethyl lactate (EtLac), ethyl acetate (EtOAc), benzyl alcohol (phiCH₂OH), a triacetin, N-methyl pyrrolidone (NMP), propylene carbonate (PC), and the Glico furol (GF) were used for these examples.

Generally it considered as the high concentration of the biological active substance in a formula object, so that there was much % of a solvent. Moreover, the amount and class of solvent also relate to the viscosity of a solution directly. Table 1 indicates the effectiveness of the solvent to SAIB / solvent mixture, and concentration. Viscosity data were obtained at 30 degrees C using the canon-Fenske viscometer of size 200.

[0057]

[Table 1]

Table 1 Matter Centipoise Distillation H₂O 1.0 EtOH 1.3 60/40 SAIB/EtOH 7.7 70/30 SAIB/EtOH 17.0 55/40/5 SAIB/EtOH/CAB 68.9 90/10 SAIB/EtOH 494.8 PC 2.1 70/30 SAIB/PC 138.7 70/30 SAIB / GURUKO furol 228.4 Peanut oil 57.8 [0058]

Effectiveness of a biological active substance Emission of drugs was proved using a methylene blue and bovine serum albumin (BSA). The biological activity compound emitted from the system included chlorhexidine, dichlofenac, DOKISAI curine, flurbiprofen, naproxen, and theophylline. Since the degree of aqueous solution of clotrimazole was low, emission was not continued.

[0059]

Example [] 1 ethanol (1g) was mixed with cane-sugar acetic-acid isobutyric-acid ester (SAIB) (9g). After mixing quietly, the transparent low viscous solution was obtained. Although one drop of this solution was underwater discharged from the glass tube and the spherical matrix was made to form, this held that configuration one week or more.

[0060]

Example [] 2 ethanol (2g) was mixed with SAIB (8g). The produced solution formed the thin film, when it mixed with water. This film held that configuration one week or more.

[0061]

Example [] 3 the amount of ethanol and SAIB was changed according to the procedure of Example 1, and the solution was prepared. 0.07% of methylene blue was added in this solution. As indicated for Example 1, the spherical drop was prepared in phosphate buffered saline (PBS). The PBS sample was held at 37 degrees C. PBS was taken out at regular spacing and it analyzed about the methylene-blue content by ultraviolet-rays-visible spectrophotometry. The result of emission of a methylene blue is shown in drawing 1.

[0062]

Example [] 4 according to the procedure of Example 3, a series of formula objects were prepared instead of the methylene blue using bovine serum albumin (BSA). Various BSAs, solvents, and SAIB(s) of % were used for these formula objects. The ratio of the additive of BSA, a solvent, SAIB, and arbitration is indicated in the body list of a solvent in the following tables 2-4. Emission of BSA became slow as the ratio of CAP:SAIB increased.

BSA was not fusibility at a system. Although it was made to solubilize using a mixed solvent and being tried as like, BSA was fusibility only at the glycerol and water which are not SAIB and a miscibility. Not all the BSA content formula objects in an emission profile were uniform. Table 2 lists the formula object containing BSA.

[0063]

[Table 2]

Table 2 %BSA %EtOH %PVP %50/50 glycerol / DMSO 4.6 36 0 5.6 5.5 36 0 5.8 5.0 33 5.9 6.9 5.5 31 8.2 8.3 4.9 27 18.8 9.8 [0064]

[Table 3]

Table 3 %BSA Solvent % solvent Additive % additive 1.1 PC 31.3 Distillation H2O 9.8 9.2 A solvent was not used (paste of BSA/SAIB).

9.6 A glycerol 9.2 - - 1.9 EtOH 30 - - 1.9 EtOH 20 - - 1.9 EtOH 10 - - 10 EtOH 10 - - [0065]

Drawing 5 illustrates the emission profile about the SAIB/BSA paste made to form, without using the solvent of any additions.

It was not obtained although the emission profile was tried from the ununiformity formula object shown in Table 4.

[0066]

[Table 4]

Table 4 %BSA Solvent % A solvent An additive % Additive 1 EtOH 9.6 - - 1 EtOH 19 - - 1 EtOH 29 - - 1 EtOH 20 - - 1 EtOH 89 - - [0067]

Example [] 5 the operating procedure of Example 3 was repeated using a series of formula objects which contain chlorhexidine as a biological activator. The formula object containing various solvents, SAIB(s), and additives of an amount was prepared.

The formula object which added chlorhexidine as a biological active substance is indicated to the following table 5.

[0068]

[Table 5]

Table Five % drugs A solvent % A solvent An additive % Additive Solubility 5 EtLac 50 - - Insoluble 30 - - Insoluble 10 - - Insoluble NMP 50 -- Soluble 30 - - Insoluble 10 - - Insoluble PC 31 -- Insoluble 20- - Insoluble 10 - - Insoluble EtOH 50 -- Soluble 30 - - Insoluble 10- - Insoluble 45 CAB5.1 Soluble 5 40 soluble 35 Insoluble 2.6 23 PVP 5.1 Insoluble 2.5 23CAB(s) 5 Insoluble 23 CAP5 insoluble -- 2.75 23 PEG (10K)5.2 Insoluble 2.4 23 PEG (1K) 5.5 Insoluble [0069]

The emission profile of the chlorhexidine in the inside of various solvents is illustrated to drawing 6 -8. The amount of fusibility of the chlorhexidine in SAIB/EtOH/CAB was optimized. A result is shown in Table 6.

[0070]

[Table 6]

Table 6 % drugs %EtOH %CAB Solubility 12 57.5 3 Insoluble (meltable, when it heats) at a room temperature

14.7 47.2 3.8 Meltable in One Day or Two Days 15 51 3.4 Insoluble 18 50.4 3.1 Insoluble [0071]

Example [] 6 the operating procedure of Example 3 was repeated using a series of formula objects which contain dichlofenac sodium as a biological activator. The formula object containing various solvents, SAIB(s), and additives was prepared. Emission of dichlofenac became slow as the ratio of CAB:SAIB increased. The formula object which added dichlofenac as a biological active substance is indicated to the following table 7.

[0072]

[Table 7]

Table Seven % drugs A solvent % A solvent An additive % Additive Solubility 2.68 EtOH 19.1 - - Insoluble 2.48 15.6 - - Insoluble 2.40 9.6 - - Insoluble 2.68 7 - - insoluble -- 2.43 7.1 cane sugars 2.6 -- insoluble 2.563.6 Cane sugar 5.1 Insoluble 2.39 28.7 CAB 4.8 Soluble 2.44 28.6 PEG4.8 (1K) Insoluble 2.89 28.7 PVP (25) 4.8 Insoluble 2.38 28.3 PEG5.3 (10K) Insoluble 2.35 36.3 CAP 5.2 Soluble 2.57 Triacetin 50 - - Insoluble 2.89 30 - - Insoluble 2.43 11.5 - - insoluble -- 2.58 DMSO 50 - - Soluble (brown)

2.45 30.5 - - Insoluble 2.36 10.2 - - Insoluble The emission profile about the dichlofenac in the inside of various solvents is illustrated to drawing 9 -12.

[0073]

Example [] 7 the operating procedure of Example 3 was repeated using a series of formula objects which contain the doxycycline as a biological activator. The formula object containing various solvents, SAIB(s), and additives of an amount was prepared. The formula object which added the doxycycline as a biological active substance is indicated to the following table 8.

[0074]

[Table 8]

Table Eight % drugs A solvent % solvent An additive % Additive Solubility 5 EtOH 15 - - Insoluble 2.56 15 - - Insoluble 4.97 EtOAc 30 - - Insoluble 2.5 EtLac 30 - - Insoluble 2.45 PC 30 - - Insoluble 2.5 GF30 - - Insoluble 2.5 DMSO 30 - - Soluble [momentary] [0075]

In order to support the solubility of the doxycycline, little DMSO was used with SAIB/EtOH/CAB mixture. These formula objects are shown in Table 9.

[Table 9]

Table 9 % doxycycline %EtOH %CAB %DMSO Solubility 3.01 49 6.7 7.6 Soluble 4.03 47 8.9 7.9 Soluble 3.07 42 5.6 7.4 Insoluble 4.17 72 21 7.5 Soluble * * SAIB use is not carried out. [0076]

Example [] 8 the operating procedure of Example 3 was repeated using a series of formula objects which contain flurbiprofen as a biological activator. The formula object containing various solvents, SAIB(s), and additives of an amount was prepared.

The formula object which added flurbiprofen as a biological active substance is indicated to the following table 10.

[0077]

[Table 10]

Table Ten % drugs A solvent % A solvent An additive % Additive Solubility 2.48 EtOH 15 - - Soluble 4.98 EtOH 15 - - Soluble 9.98 EtOH 15 - - Soluble 4.99 EtOH 45 CAB 5.0 Soluble 9.92 EtOH 45 CAB5.5 Soluble The emission profile about flurbiprofen is shown in drawing 13 .

[0078]

Example [] 9 the operating procedure of Example 3 was repeated using a series of formula objects which contain naproxen (free acid) as a biological activator. The formula object containing various solvents, SAIB(s), and additives of an amount was prepared.

The formula object which added naproxen (free acid) as a biological active substance is indicated to the following table 11.

[0079]

[Table 11]

Table Eleven % drugs A solvent % A solvent An additive % additive Solubility 5.2 GF 21 -- Soluble 3.6 GF 37 -- Soluble 4.1 GF 44 -- Soluble [0080]

Example [] 10 the operating procedure of Example 3 was repeated using a series of formula objects which contain naproxen (sodium salt) as a biological activator. The formula object containing various solvents, SAIB(s), and additives of an amount was prepared.

Naproxen (sodium salt) is not fusibility at EtOH and EtOH. The formula object which added naproxen (sodium salt) as a biological active substance is indicated to the following table 12.

[0081]

[Table 12]

Table Twelve % drugs A solvent % Solvent Additive % additive Solubility 5.2 GF 21 -- Insoluble 3.4 GF 37 -- Soluble 3.9 GF 44 -- Soluble The emission profile about the naproxen (a free acid and sodium salt) in the inside of various solvents is shown in drawing 14.

[0082]

Example [] 11 the operating procedure of Example 3 was repeated using a series of formula objects which contain naproxen (sodium salt) and naproxen (free acid) as a biological activator. The formula object containing various solvents, SAIB(s), and additives of an amount was prepared.

The formula object which added naproxen (sodium salt) and naproxen (free acid) as a biological active substance is indicated to the following table 13.

[0083]

[Table 13]

Table 13 % free acid % Na salt A solvent % A solvent Solubility 2.38 2.55 PC 20 Soluble 1.28 3.56 GF 20 Insoluble 2.27 2.78 EtLac 30 Soluble 2.49 2.55 GF 20 Soluble [0084]

Example [] 12 the operating procedure of Example 3 was repeated using a series of formula objects which contain theophylline as a biological activator. The formula object containing various solvents, SAIB(s), and additives of an amount was prepared. The formula object which added theophylline as a biological active substance is indicated to the following table 14.

[0085]

[Table 14]

Table 14 % drugs A solvent % A solvent Additive % additive Solubility 0.5 EtOH 15 -- Insoluble 1 EtOH 15 -- Insoluble 2.5 EtOH 15 -- Insoluble 5 EtOH 15 -- Insoluble 10 EtOH 15 -- Insoluble 2.5 EtOH 53 CAB 5 Insoluble 2.5 EtOH 47 CAB 10 Insoluble 2.5 EtOH 43 CAB 15 Insoluble 2.5 EtOH 53 CAP 5 Insoluble 2.6 EtOH 48 CAP 10 Insoluble 2.5 EtOH 43 CAP 15 -- insoluble 5.2 EtOAc 48 -- Insoluble 4.8 EtOAc 29 -- Insoluble 5.0 EtOAc 9.5 -- Insoluble 5.0 phitCH₂OH 48 -- insoluble 5.2 phitCH₂OH 29 -- Insoluble 5.0 phitCH₂OH 11 -- Insoluble 5.4 EtOH 10 -- Insoluble 6.5 EtOH 20 -- Insoluble 5.5 EtOH 30 -- Insoluble 5.5 EtOH 25 CAB 5.5 Insoluble 7.2 EtOH 34 CAB(s) 5.4 Insoluble 5.4 EtOH 45 CAB 5.9 Insoluble 5.1 PC 11 -- Insoluble 5.5 PC 20 -- Insoluble 5.5 PC 31 -- Insoluble [0086]

The emission profile about the theophylline in the inside of propylene carbonate is shown in drawing 16.

Although the emission profile was tried with the method of profit about the following formula object containing theophylline, the sample had become muddy very much. The amount of the matter in these formula objects is shown in the following table 15.

[0087]

[Table 15]

Table 15 % drugs A solvent % Solvent Additive % Additive Solubility 4.9 EtOH 16 PVP (K25) 5.1 Insoluble 5.0 EtOH 40 PVP (K25) 5.0 Insoluble 5.1 EtOH 15 PEG (1K) 5.0 Insoluble 5.0 EtOH 40 PEG (1K) 5.0 Insoluble 4.9 EtOH 16 PEG 5.4 (10K) Insoluble 4.9 EtOH 41 PEG (10K) 4.9 Insoluble [0088]

Example [] 13 the formula object was prepared using 80% of SAIB, and 15% of ethanol, and the aerosol container was loaded with the obtained solution. This solution was sprayed on the agar plate and

the adhesive continuation film was formed there.

[0089]

Example [] 14 80% of SAIB, and 0.02% of methylene blue -- using it -- an ethanol pair -- the ratio of CAB was changed into 1:1 from 1:0, and a series of formula objects were prepared. The formula object was sprayed on gelatin. Rarefaction of the methylene blue to the inside of gelatin became slow when the CAB content increased.

[0090]

Example [] 15 SAIB was heated at 60 degrees C. Another formula object was prepared using 1, 2, 5, and 10% of tetracycline. The syringe equipped with the needle of 21 gages was loaded with these formula objects. The formula object was made to discharge manually in 37-degree C butter from a syringe. The formula object was able to be made to discharge easily at the temperature of about 45 degrees C.

[0091]

Example 16: manufacture and the property of a gargle A polyoxyethylene (7.680g, 20EC) almond oil (Crovol A-70), 4.042g deca glycerol tetra-oleate (Caprol IOG40), and the inside chain triglyceride (Neobee M-5) of 11.721g were mixed in the suitable mixed container (jacket, single operation, and surface cleaning kettle). Mixture was heated at about 65 degrees C. Methyl PARABAN (0.500g), 0.250g propyl PARABAN, 0.125g cetylpyridinium chloride, a 0.125g benzoic acid, and 0.625g cane-sugar acetic-acid isobutyric-acid ester were made to mix in the heated organic phase. Organic phase mixture was held at about 65 degrees C all the time during addition of a component. Zinc gluconate (0.250g), a 0.125g sodium benzoate, the acid that cannot go away 0.0625g, and 12.5g sorbitol were dissolved in 221.10g deionized water. Aqueous-phase mixture was heated at about 65 degrees C. After the both sides of an organic phase and aqueous-phase mixture reached predetermined temperature, it added slowly, stirring the aqueous phase to an oil phase. When the aqueous phase was completely added to an oil phase, two drops of green food colors and 1.000g peppermint oil were mixed, and it fully mixed, and considered as the formula object. Subsequently, mixture was quenched and packed to the room temperature. The water lost during processing on this scale is about 10.1g. The finished product has the following presentation.

[0092]

[Table 16]

Table 16 Component A weight % PEG-20 almond oil 3.07 Inside chain triglyceride 4.69 Deca glycerol tetra-oleate 1.62 Water 84.4 Peppermint oil 0.400 Methyl PARABAN 0.200 Propyl PARABAN 0.100 Cetylpyridinium chloride 0.050 Zinc gluconate 0.100 Sorbitol 5.00 Sodium benzoate 0.050 Citric acid 0.025 Benzoic acid 0.050 [0093]

Example [] 17 the piece of a vascular transplant was immersed in the solution of 61.8% of SAIB which added 1% of heparin, 10.0% of CAB, and 28.2% of EtOH. The solution was removed from the transplant and it rinsed with the physiological saline. The piece of a vascular transplant was transplanted to the dog. After explantation, the inner surface of a transplant did not contain the solidified blood compared with the piece of the example vascular transplant of contrast.

[0094]

Example [] 18 5% of CAB, 45% of ethanol, and the formula object of 50% of SAIB were prepared. To these, it is 0.05 - 0.0005% of amount about transformation growth factor-beta, or the phenol was added in 1 - 5% of range. The inguinal canal of a dog was injected with these constituents, they pulled out the cell reaction there, and lock out of an inguinal canal was brought about.

[0095]

Example [] 19 the aerosolization of 10% of CAB, 45% of ethanol, and the formula object of 45% of SAIB was carried out to the uterine horn of the rabbit which ***** made surgical. Although the front face did not show all exclusion of surgical adhesion by reexamination, the body was biologically tolerant fully.

[0096]

example 20 Drawing 17 is the graph of emission of two sorts of formula objects. One formula object

(black shading) contains 3.2% of SAIB, 15.1% of EtOH, and 0.00395% of methylene blue, and the remainder is distillation H₂O. The formula objects (it is shading with a slash) of another side were 0% of SAIB, 28.9% of EtOH, 0.00395% of methylene blue, and distillation H₂O.

The 1 inch natural collagen strip was cut, and it is among PBS (pH6.8), rinsed, was immersed for 9 minutes into the formula object, put into the pure test tube, and covered by PBS. When it differed, the decantation of PBS was carried out and W-analysis was performed. PBS fresh to the test tube containing a collagen was added. Please refer to drawing 17.

[0097]

Example [] 21 block of surgical adhesion The solution which contains 80% of the weight of SAIB in 2-pyrrolidone is prepared. This solution is filtrated aseptically in the bottle equipped with the aerosol pump head. A surgery into the trap and this solution are sprayed on the front face of the uterine horn which ***** of a rabbit carried out. This sample was inspected in respect of the both sides of a number and violence about reduction of surgical adhesion compared with the example of brine contrast. [0098]

Example [] 22 block of surgical adhesion The solution which contains 60% of the weight of SAIB and 10% of the weight of a carboxymethyl cellulose in 30% of ethanol is prepared. It sprays on the front face on which ***** of the cecum of a rat carried out the aerosol spray of this solution, and a film is made to form there. This sample was inspected about reduction of surgical adhesion.

[0099]

Example [] 23 application to restoration of an opening The solution which contains 85% of SAIB in ethanol is prepared. Poured this solution into the interior of the blood vessel which has assigned a neoplasm, it was made to precipitate to viscous gel there, and supply of blood was made to blockade. This sample was inspected about the necrosis in which the neoplasm of 24 hours after was conspicuous.

[0100]

Example [] 24 application to restoration of an opening The solution which contains 85% of SAIB in ethanol is prepared. This solution is poured into the opening which remained after removal of a solid neoplasm.

[0101]

Example [] 25 rebirth of an induction organization The solution which contains 75% of the weight of SAIB in propylene carbonate is prepared. This solution is applied to the organization chart side after the debridement of **** surgery into the trap. This sample was inspected about reduction of the epithelial migration which produces the shallow parodontal pocket compared with the example of contrast.

[0102]

Example [] 26 application to hemostasis SAIB is mixed with 25% of the weight of polyvinyl alcohol, and a thick paste is formed. Newly cut, and apply this paste on the surface of a sternum, it was made to adhere, and the further blood flow was stopped.

[0103]

Example [] 27 prepare the solution which contains 75% of the weight of SAIB in ethyl lactate. Sprayed on the front face from which this solution was cut in the open heart surgery, the thin film was made to form, and the blood flow was stopped.

[0104]

Example [] 28 application to fusion of an organization The solution which contains 75% of the weight of SAIB in a N-methyl-2-pyrrolidone is prepared. This solution is sprayed on the inner surface of the abdominal wall of the rat in front of closing of a surgery after the operation. The suture which takes this sample to ensure closing of suitable incision compared with the undisposed example of contrast inspected about the proof of few things.

[0105]

Example [] 29 application to SUKAHORUDINGU The formula object containing 75% of SAIB, 15% of polyvinyl pyrrolidone, and 10% of phosphoric acid TORIKARUSHIUMU is prepared. When it was used for holding bone chips collectively and a new bone was formed in the neck bone which had this paste destroyed, it inspected about the proof of late absorption.

Prepared another formula object, bone morphogenesis nature protein (BMP) was made to contain, and it

inspected about the proof of early recovery compared with the example of contrast which does not contain BMP.

The formula object which consists of 65% of SAIB, 10% of Pori (lactide-KOGURI corridor), 5% of polyethylene glycol, and 20% of propylene glycol is prepared. It applies, before suturing on the front face of the ligament which had this solution torn. This sample was inspected about early recovery compared with the example of contrast.

[0106]

Example [] 30 allowance material of a wound The solution which comes to dissolve SAIB in Dymel was prepared by cooling Dymel(trademark) 134 a/P drugs grade HFC-134a propellants (trademark of JUPON) in a dry ice bath, and adding to the amount adjusted to the pressure bottle beforehand loaded with SAIB. The transparent solution was able to be obtained when temperature was raised to the room temperature. This solution is sprayed on the wound of sufficient thickness of Buta, and a transparent coherent film is brought about there. This sample was inspected about a low infection rate and early recovery compared with gauze or the undisposed example of contrast. Another wound allowance material contained 5% of the weight of amikacin, or 0.02% of elementary fiber blast cell growth factor. Conditioning of the standard cotton gauze is carried out with the aerosol of SAIB in ethanol, or it is immersed in the ethanol solution of SAIB. Ethanol is evaporated from gauze. The gauze and the unsettled gauze which were processed are placed on the skin wound of the back of Buta. It inspected about closing of the wound earlier than unsettled gauze about the gauze which processed this sample by SAIB.

[0107]

Correction and deformation of the constituent of this invention and its use will become whether to be ** from the above-mentioned detailed explanation at this contractor. Such correction and deformation are required within the limits of this invention.

[Brief Description of the Drawings]

[Drawing 1]

It is the graph of emission of the methylene blue from SAIB (cane-sugar acetic-acid isobutyric-acid ester) when measuring by rate of emission % about time amount (hr) (80% of SAIB, round-head; 85% black SAIB, a downward black trigonum; 90% of SAIB, white rectangular-head; 95% SAIB, upward trigonum).

[Drawing 2]

It is the graph of emission of the theophylline from SAIB when measuring by the burst size (mg/mg) about time amount (hr) (0.5% of theophylline, round-head; 1.0% black theophylline, downward triangular; 2.5% theophylline, black rectangular-head; 5.0% theophylline, a upward trigonum; 10% of theophylline, filled diamond).

[Drawing 3]

The effectiveness of cane sugar over the emission of the methylene blue from 90%SAIB when measuring by rate of emission % about time amount (hr) is illustrated (a black round head, 0% of cane-sugar (90%SAIB, 10%EtOH); facing-down trigonum, 2.5% of cane sugar (90%SAIB, 7.5%EtOH); a black rectangular head, 5.0% of cane sugar (90%SAIB, 5%EtOH)).

[Drawing 4]

The effectiveness of CAB (cellulose acetic-acid butylate) to emission of the methylene blue from SAIB when measuring by rate of emission % about time amount (hr) is illustrated (a black round head, 5% of CAB (SAIB40%, EtOH55%); a downward black trigonum and 10% of CAB(SAIB40%, EtOH50%); a black rectangular head, 15% of CAB (SAIB40%, EtOH45%)).

[Drawing 5]

It is the graph of emission of BSA from BSA (9%) / SAIB paste when measuring by the burst size (mg) about time amount (hr).

[Drawing 6]

It is the graph of emission of the chlorhexidine from SAIB/ethyl lactate (EtLac) when measuring by rate of emission % about time amount (hr) (50/50 of SAIB/EtLac, a white round head; 70/30 of SAIB/EtLac,

downward white triangular;90/10 SAIB/EtLac, white rectangular head).

[Drawing 7]

It is the graph of emission of the chlorhexidine from SAIB/NMP when measuring by rate of emission % about time amount (hr) (50/50 of SAIB/NMP, white SAIB/NMP of round-head;70/30, a downward white trigonum; 90/10 of SAIB/NMP, white rectangular head).

[Drawing 8]

It is the graph of emission of the chlorhexidine from SAIB/propylene carbonate when measuring by rate of emission % about time amount (hr) (64% of SAIB, a white round head; 75% of SAIB, downward white triangular;85%SAIB, white rectangular head).

[Drawing 9]

It is the graph of emission of 2.5% dichlofenac from SAIB/triacetin when measuring by rate of emission % about time amount (hr) (50/50 of SAIB/triacetins, white white SAIB/triacetin of round-head;70/30, a downward white trigonum; 90/10 of SAIB/triacetins, white rectangular head).

[Drawing 10]

it is the graph of emission of 2.5% dichlofenac from SAIB/ethanol (EtOH) when measuring by rate of emission % about time amount (hr) (an implication and this are not included for cane sugar) (it SAIB(s) 79% --) A rectangular-head;82% white SAIB, a downward triangular;90% black SAIB, a rectangular-head;88% black SAIB, downward white triangular;88% SAIB, 2.5% of cane sugar, a black round head; 80% of SAIB, 5% of cane sugar, a white round head.

[Drawing 11]

It is the graph of emission of 2.5% dichlofenac from SAIB/EtOH (they are CAB of an additive, and those with cellulose acetic-acid propionic-acid ester ("CAP") to an additive-less list) when measuring by rate of emission % about time amount (hr) (additive nothing, those white with rectangular-head;CAP, those with downward white triangular;CAB, white round head).

[Drawing 12]

It is the graph of emission of 2.5% dichlofenac from SAIB/dimethyl sulfoxide (DMSO) when measuring by rate of emission % about time amount (hr) (70/30 of SAIB/DMSO, a white round head; 90/10 of SAIB/DMSO, downward white trigonum).

[Drawing 13]

It is the graph of emission of the flurbiprofen from SAIB/45%EtOH/5%CAB when measuring by rate of emission % about time amount (hr) (4.99% of flurbiprofen, a white rectangular head; 9.92% of flurbiprofen, filled diamond).

[Drawing 14]

it is the graph of emission of the naproxen (a free acid or sodium salt) from SAIB / Glico furol when measuring by rate of emission % about time amount (hr) (it SAIB(s) 73% --) 5.2% of naproxen (free acid), a white round head; 60% of SAIB, 3.6% of naproxen (free acid), Downward white trigonum; 52% of SAIB, 4.1% of naproxen (free acid), rectangular-head;74% white SAIB and 5.2% of naproxen (sodium salt) -- round-head;60% black SAIB, 3.4% of naproxen (sodium salt), downward triangular;52% black SAIB, 3.9% of naproxen (sodium salt), and a black rectangular head.

[Drawing 15]

It is the graph of emission of 2.5% theophylline from SAIB(40%)/EtOH/CAB or CAP when measuring by rate of emission % about time amount (hr) (5% of CAB, a round-head;10% white CAB, a round-head;15% black CAB, a downward white triangular;5% CAP, downward triangular;10% black CAP, a white rectangular head; 15% of CAP, black rectangular head).

[Drawing 16]

It is the graph of emission of the theophylline from SAIB/propylene carbonate when measuring by rate of emission % about time amount (hr) (64% of SAIB, downward white triangular;74% SAIB, a black round head; 84% of SAIB, white round head).

[Drawing 17]

It is the graph of emission of two sorts of formula objects. One formula object (black shading) contains 3.2% of SAIB, 15.1% of EtOH, 0.00395% of methylene blue, and the remaining distillation H2O. The

formula object (shading of a slash) of another side contains 0% of SAIB, 28.9% of EtOH, 0.00395% of methylene blue, and the remaining distillation H₂O.

[Translation done.]

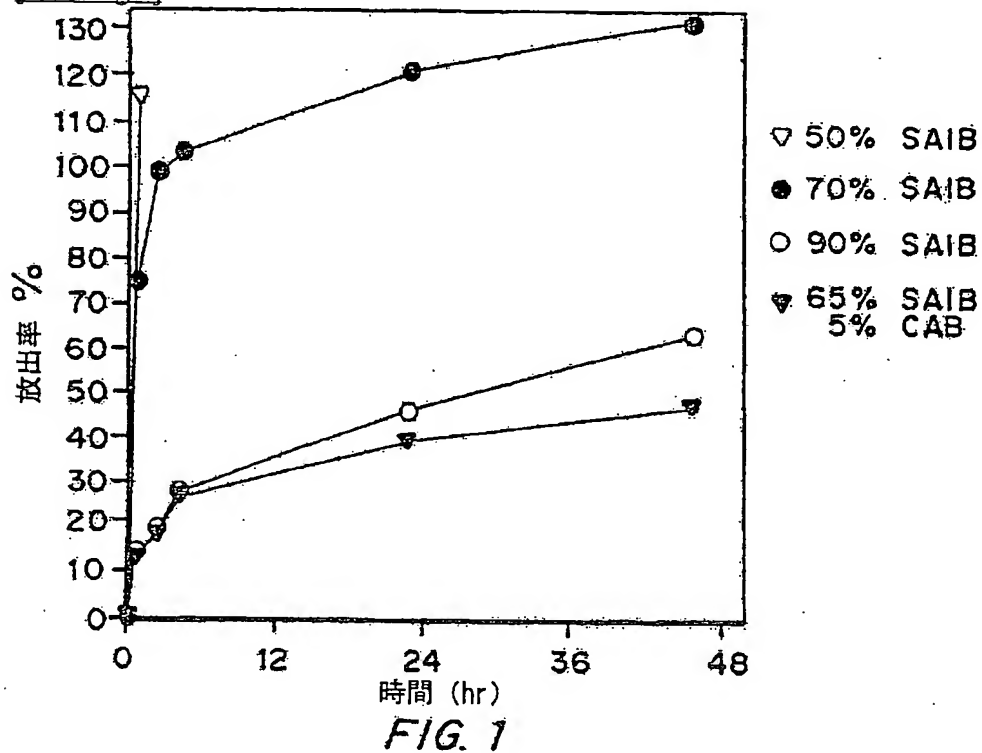
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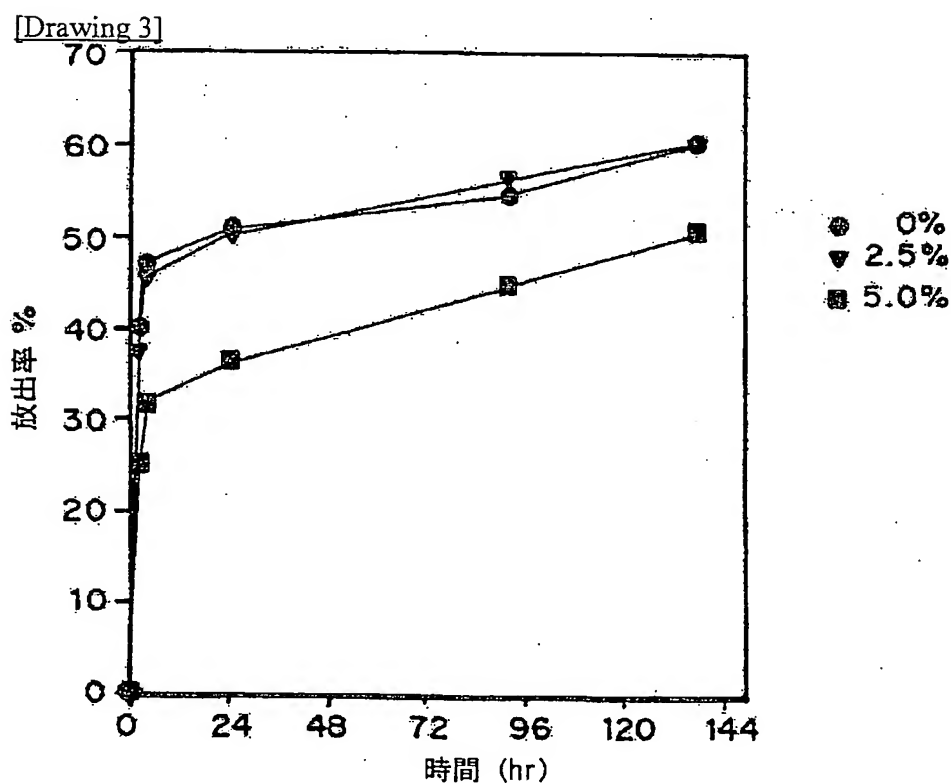
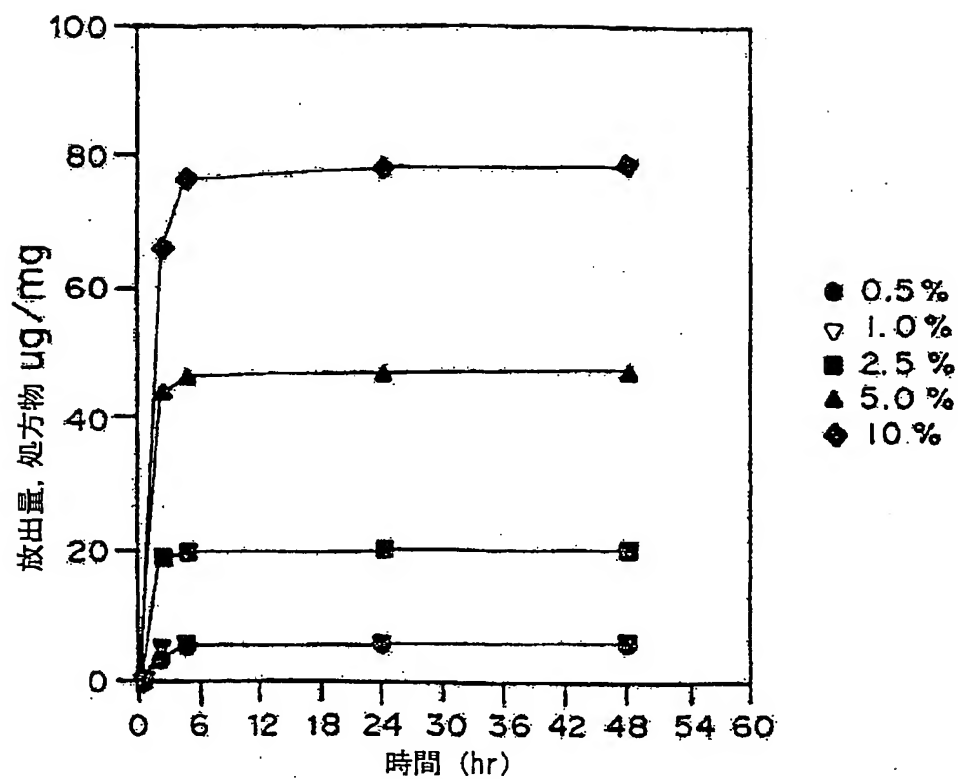
1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. **** shows the word which can not be translated.
3. In the drawings, any words are not translated.

DRAWINGS

[Drawing 1]



[Drawing 2]



[Drawing 4]

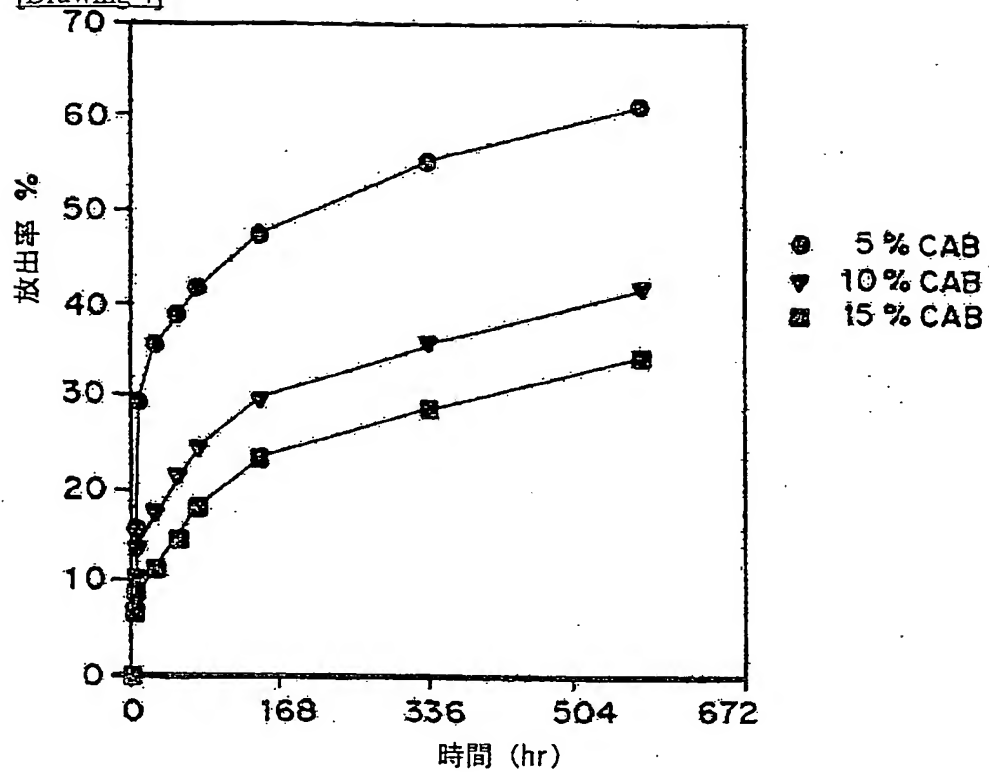


FIG. 4

[Drawing 5]

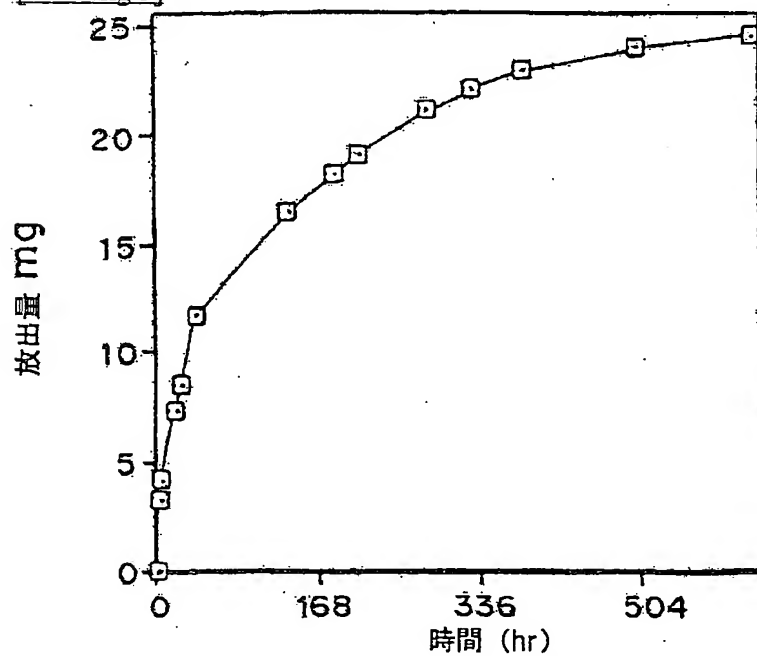


FIG. 5

[Drawing 6]

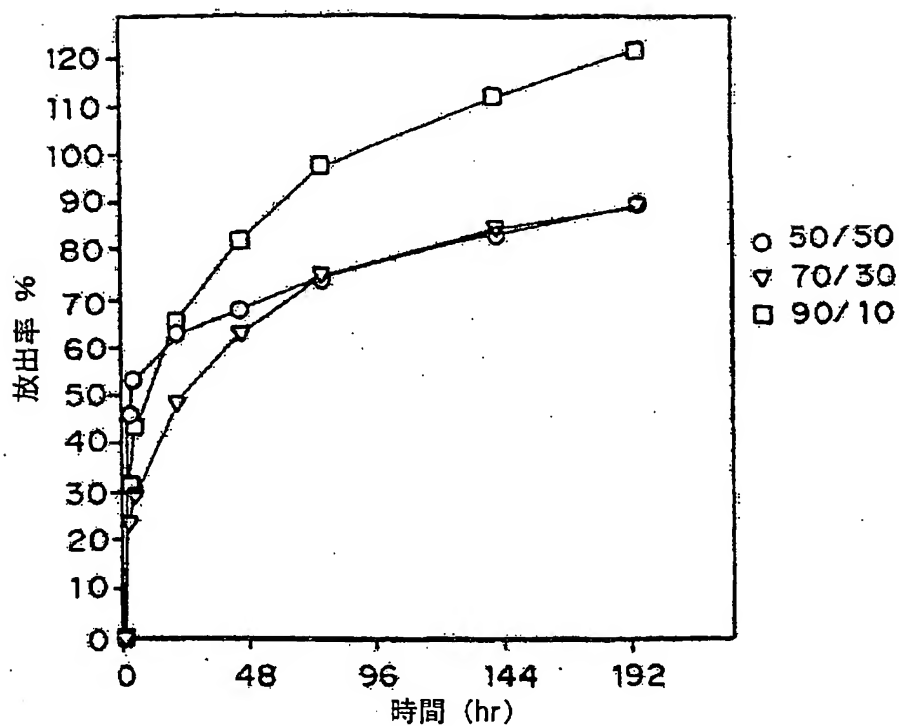


FIG. 6

[Drawing 7]

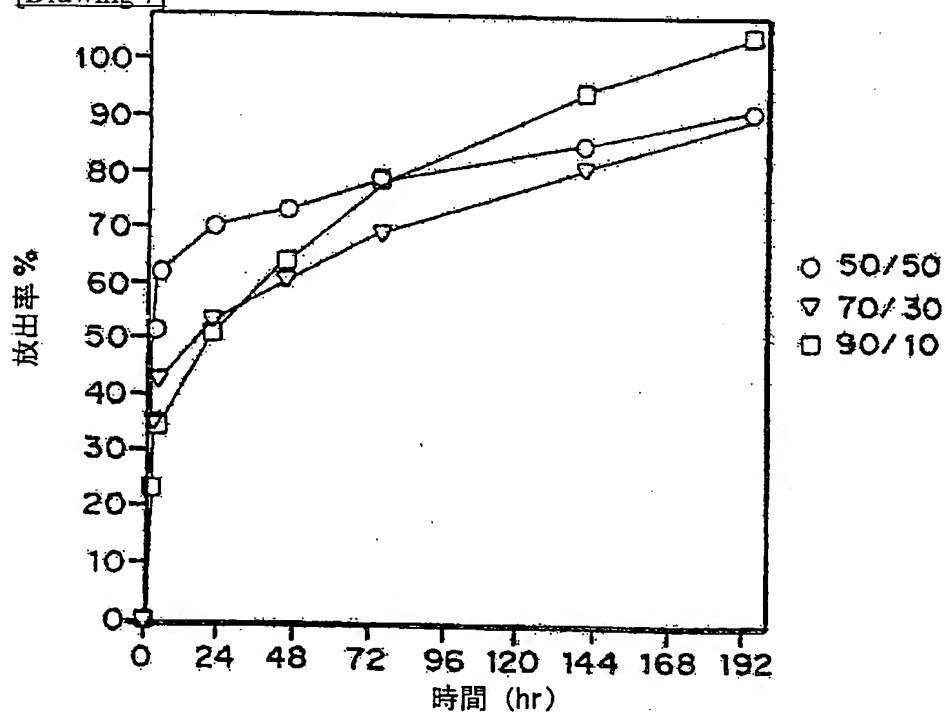


FIG. 7

[Drawing 8]

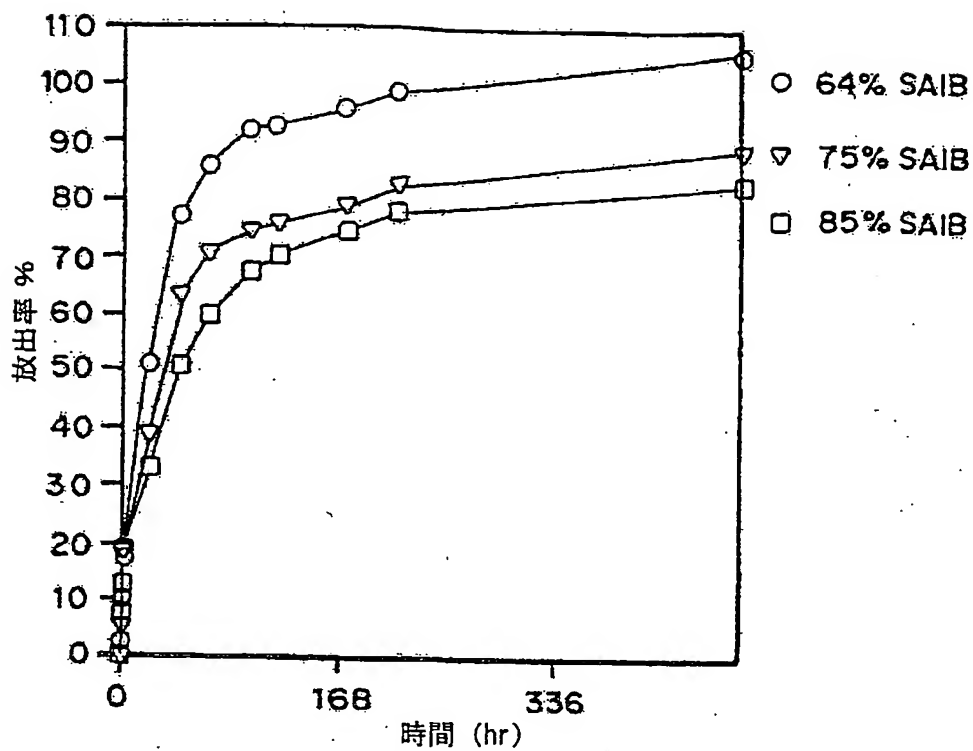


FIG. 8

[Drawing 9]

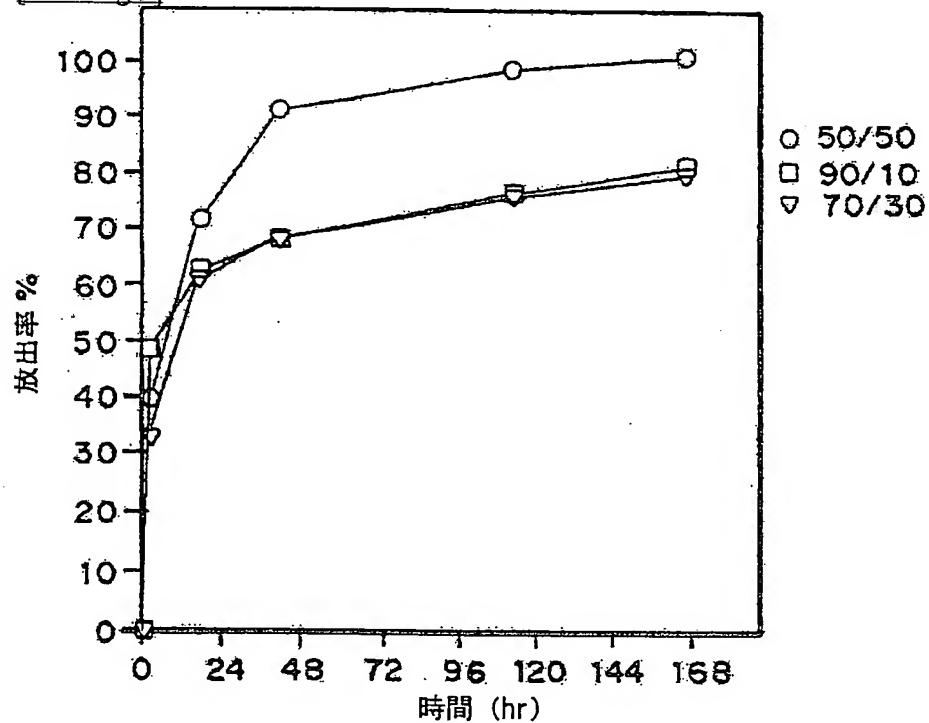


FIG. 9

[Drawing 10]

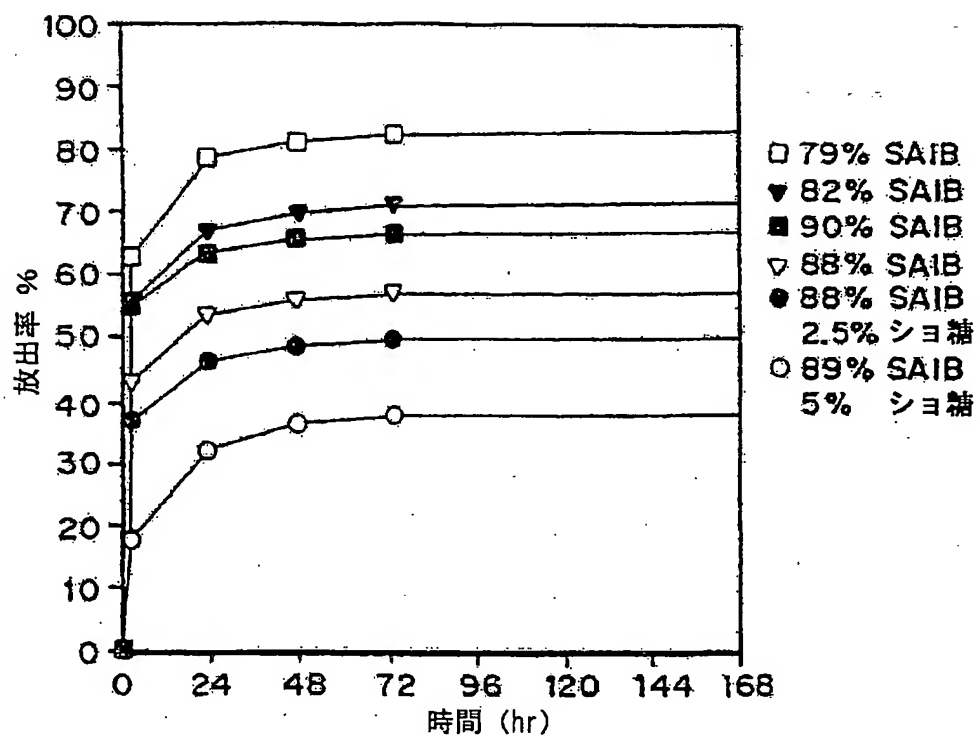


FIG. 10

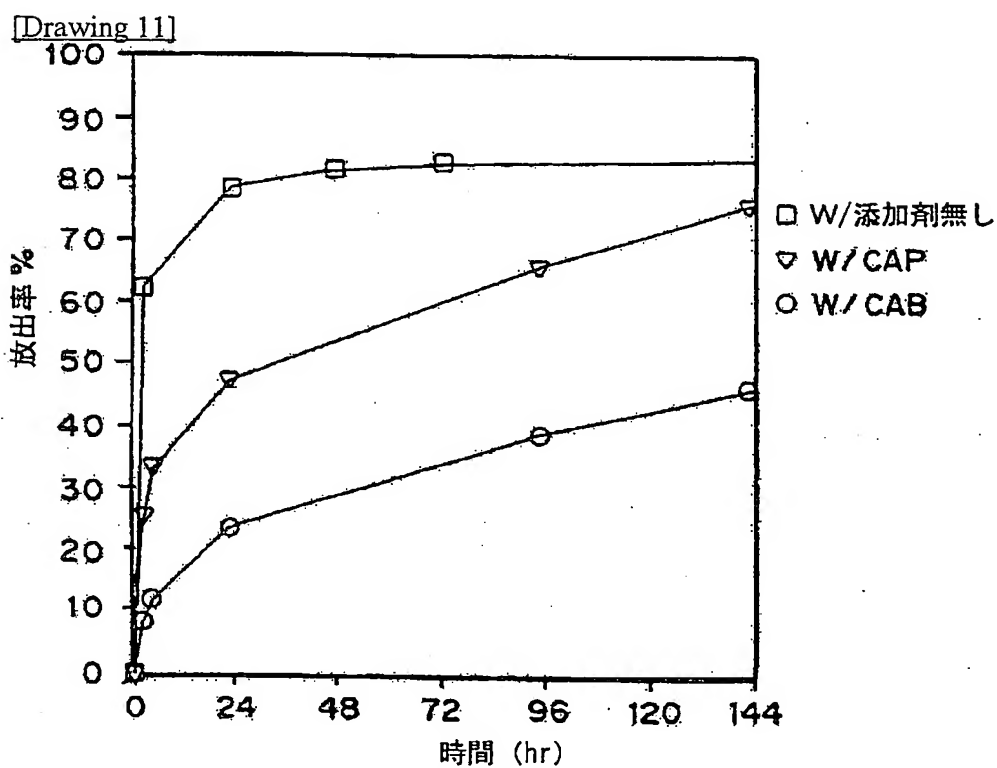


FIG. 11

[Drawing 12]

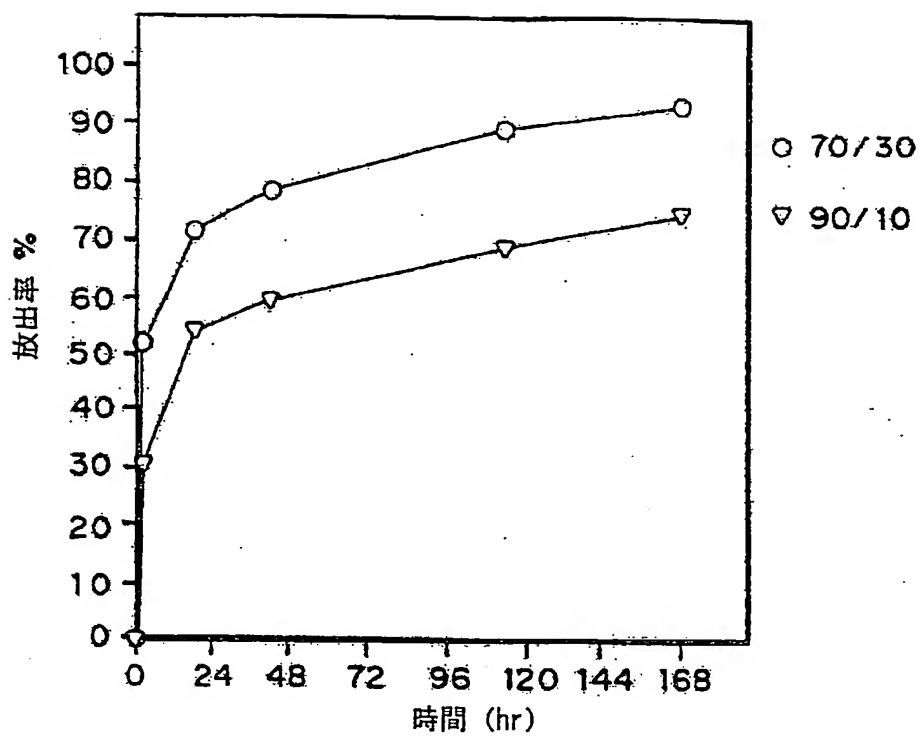
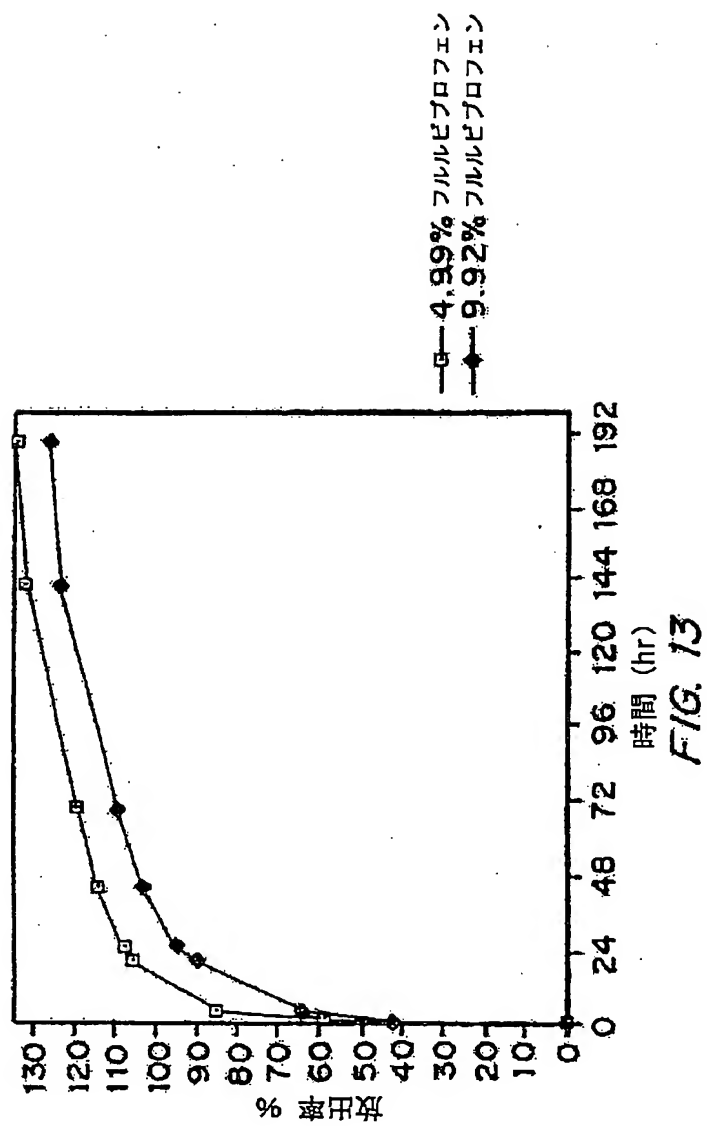
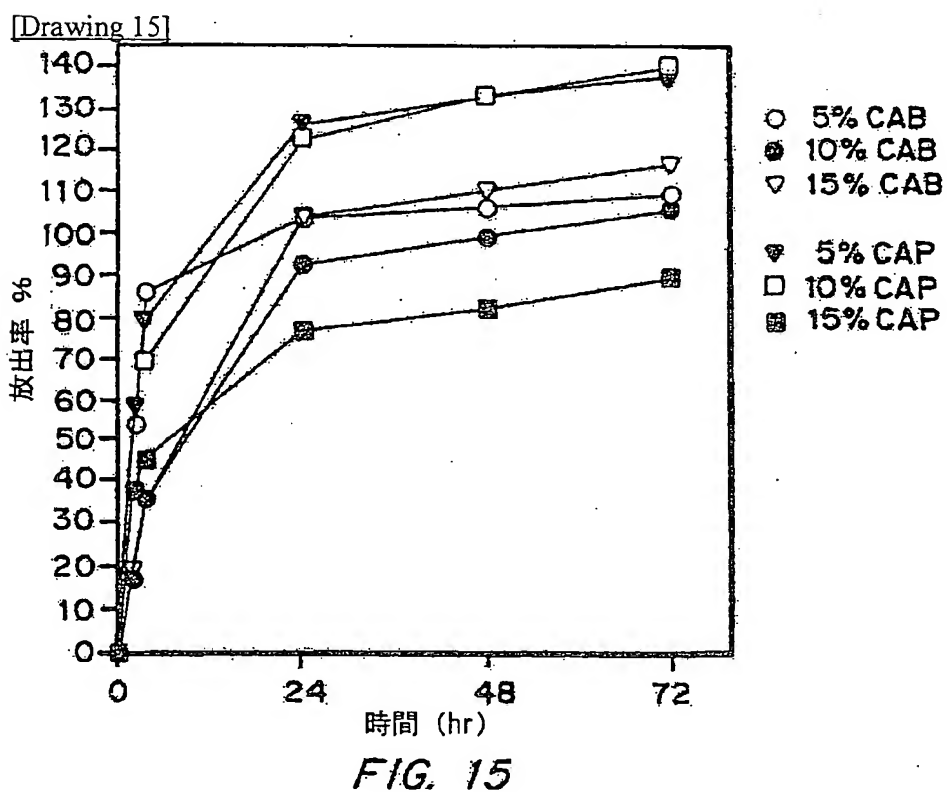
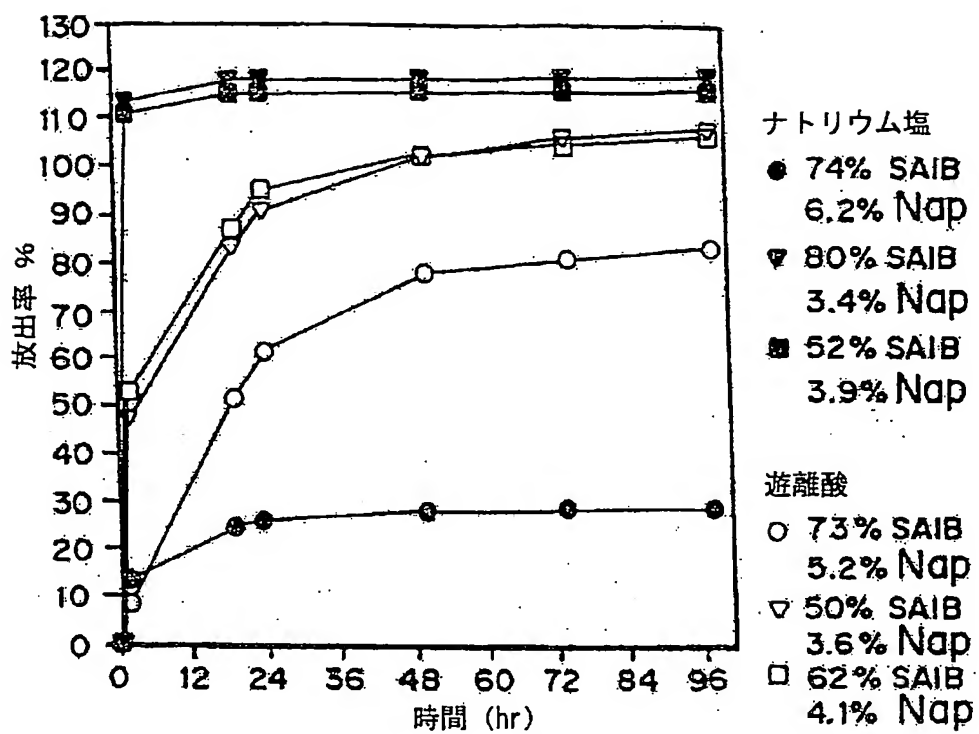


FIG. 12

[Drawing 13]



[Drawing 14]



[Drawing 16]

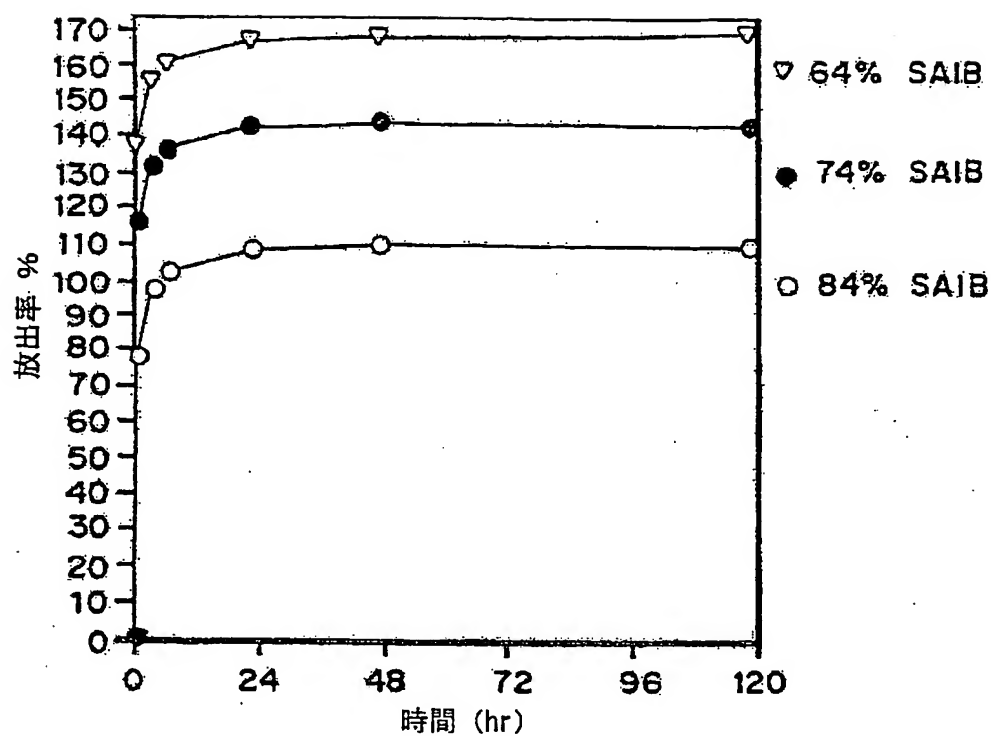


FIG. 16

[Drawing 17]

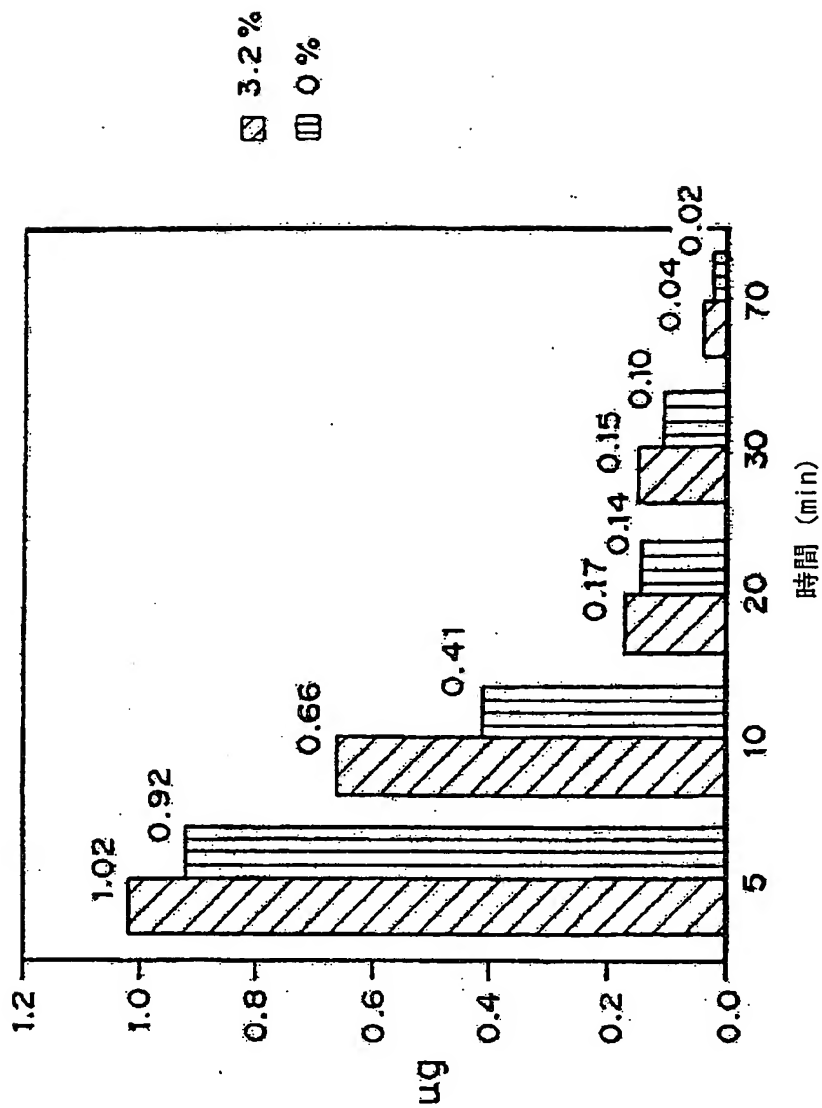


FIG. 17

[Translation done.]